ACUTE EFFECTS OF SLEEP DEPRIVATION ON OCULAR-MOTOR FUNCTION AS ASSESSED BY KING-DEVICK TEST PERFORMANCE

By

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Thank you to McCarthy “Mac” Ferris, Ryan Krueger, and Mitchell Meyer for spending nights at the School of Public Health supervising participants and for being good sports as I learned how to mentor and manage students in research.

Thank you to my parents, Robert and Therese, and brother, Ben, for their emotional support and for trying to understand my research simply because it is my passion and took so much of my time.

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ABSTRACT

Less than 10% of high school and college student-athletes obtain the recommended amount of sleep each night. Ocular-motor function, specifically saccade movement, is known to be negatively affected by sleep deprivation. The King-Devick Test is a concussion assessment tool that measures neurocognitive and saccadic function. However, how one's King-Devick Test performance is affected by sleep deprivation remains unknown. Thus, the purpose of this study was to investigate the acute effects of sleep deprivation on ocular-motor function as assessed by the King-Devick Test. We hypothesized that those who were sleep deprived would have an increased, or worsened time performance in the King-Devick Test compared to those in the control group.

Forty-two college-aged subjects (18-26 years old) who regularly slept 7-9 hours per night and had normal or corrected-to-normal vision were recruited in the study. Exclusion criteria were any sleep disorders or neurocognitive dysfunctions, and pregnant females. Participants were randomly assigned to one of 2 groups: control and sleep deprivation. One week prior to testing, participants were fitted with an ActiGraph and given a sleep log to objectively and subjectively record sleep durations, respectively. There were 3 test sessions with 1 intervention over a 24-hour period: Test 1 (7am), Test 2 (7pm), overnight sleep intervention, Test 3 (7am). King-Devick measurements of time in seconds and cumulative errors made were recorded for each test session. Individuals in the sleep deprivation group underwent sleep restriction of 3.5 hours during the intervention while the control group slept 8 hours. A repeated measures analysis of variance was used to identify a significant time by group interaction as well as main effect for time. Further investigation using Bonferroni post-hoc testing allowed insight to the significant difference(s) that

occurred. Data were analyzed using SPSS Statistics Version 23 and level of statistical significance was set to $P< 0.05$.

The repeated measures analysis of variance showed that there was a statistically significant Group x Time interaction for King-Devick speed, [$F_{(1.7,67.6)}$=8.840, p=0.001], and showed significant main effect for time [$F_{(1.7,67.6)}$=12.736, p <0.001]. Bonferroni post-hoc analysis revealed that the control group continued to improve their saccadic performance over time [Time 1 (42.0±4.4), Time 2 (40.2±4.2), Time 3 (38.4±4.2); Time 1 vs. 2, p<0.001; Time 1 vs. 3, p<0.001; Time 2 vs. 3, p=0.028], while such improvement was not seen in the sleep deprivation group after acute sleep deprivation [Time 1 (41.3±5.8), Time 2 (38.7±6.0), Time 3 (40.9±7.3): Time 1 vs. 2, p<0.001; Time 1 vs. 3, p=1.00; Time 2 vs. 3, p=0.002].

In conclusion, acute sleep deprivation mitigates learning effect seen in the control group, indicating that acute sleep deprivation may cause substantial decrease in neuro-ophthalmologic efficiency. Sleep deprivation negatively impacts ocular-motor function, specifically saccadic movement, as illustrated by regressing expected learning curve in the King-Devick perfromance in the sleep deprivation group. Relying on saccades and cognitive function, the King-Devick Test is a commonly used concussion assessment tool. The result has an immense clinical implication because administering the King-Devick Test to someone in a sleep deprived condition may falsify the results. A baseline test could be inaccurately high which, when compared to a post-injury result, may create a false negative. Further, a post-injury test in a sleep deprived condition may increase the performance time even in the absence of a concussion leading to a false positive.

THESIS MANUSCRIPT

INTRODUCTION

Sleep deprivation is an epidemic phenomenon affecting millions of people. In the United States, only 7.6% of secondary school students are meeting the ideal sleep goal of nine hours per night for adolescents.[1-3] In fact, by interviewing 3476 students in 8th grade and 10th grade, Paiva and colleagues[3] found that a habit of reduced sleep duration worsens as students progress through their schooling. Researchers attribute the prevalent sleep deprivation to varying biological and social factors, including employment status, social interaction, caffeine consumption, and age or stage of life.[1, 2] The causes of sleep deprivation vastly vary, yet outcomes are consistent that without sleep one can expect to experience detrimental side effects to mental and physical health both acutely (e.g., headache, fatigue, depressed mood, increased irritability and difficulty concentrating)[1, 4] and chronically (e.g., diabetes, hypertension, obesity).[2] Additionally, sleep deprivation causes neurological impairment such as decreased alertness, reaction times, and cognitive function.[5, 6] Emerging evidence has shown that a neuro-ophthalmologic circuit is particularly sensitive to a lack of sleep.[7, 8]

Vision and ocular-motor functions are linked to multiple aspects of brain function and have been identified as a practical and reliable means of assessing brain function.[7-9] [10-12] In particular, saccades, may be particularly sensitive to sleep deprivation as they are chiefly controlled by the cranial nerves: oculomotor (III), trochlear (IV), and abducens (VI), with accessory information derived from the basal ganglia, frontal lobe, and cerebellum of the brain.[13, 14] Most dominant muscular control of the eye for saccades comes from the lateral rectus muscle. Saccadic eye movements are often measured in the form of a velocity, spatial acceleration, and accuracy. There are two types of saccades: voluntary and reflexive. Voluntary saccades are made with the intention of a goal, while a reflexive saccade are involuntary response to sudden appearance of an object in

the field of vision.[15] With the saccadic eye movements combined with the cognitive function of reading numbers aloud, the King-Devick Test (KDT) examines the function of multiple facets of the brain including eye fields (frontal eye fields, supplementary eye fields), dorsolateral prefrontal cortex, cerebellum, cerebral cortex, and deeper structures of the brain stem.[7, 8, 16] The KDT isolates saccades as the only ocular-motor function under examination in the test due to the rapid succession of focusing on one numerical figure to the next,[11] requiring a total of nearly 2,500 horizontal saccades and 371 oblique saccades to complete the test.[17]

Currently, there is a lack of literature examining the acute effects of sleep deprivation on KDT performance time. The present study aims to fill that knowledge gap by examining the effects of 20-hours of sleep deprivation on saccadic performance as assessed by the KDT. The central hypothesis is that there will be a deterioration of performance in the sleep deprived group from baseline testing compared to a regularly sleeping control group after 20-hours of wakefulness. Additionally, a secondary hypothesis is that all participants will demonstrate a learning effect or bettered performance, as discussed in previous research.

METHODS

Subjects

Healthy college-aged individuals, ages 18-26 years, were recruited to participate in this study. Subjects were randomly assigned to either sleep deprivation or control group. Inclusion criteria were between 18-26 years old, had normal or corrected-to-normal vision (minimum 20/30), and slept an average of 7-9 hours per night for one week. Participants were excluded if they have any neurocognitive dysfunctions and/or sleep disorders. Females were excluded if they were pregnant.

After completion of informed consent, participants were given a subjective sleep log to complete and fitted with ActiGraph wGT3X-BT (Pensacola, FL) to objectively monitor sleep activity for 7 days prior to the testing sessions. The use of this monitor ensured an objective testimony to the subject-reported average sleep amount. Also, prior to Test 1, a Snellen eye chart was used to validate participants' normal or corrected-to-normal vision (minimum 20/30).

Study Design

A repeated measures design was used to uncover the effects of sleep deprivation on KDT performance. The independent variables were group at two levels (sleep deprivation and control) and time at three levels (7:00AM Day 1, 7:00PM Day 1, 7:00AM Day 2). The dependent measurement was the cumulative time in seconds it takes participants to complete the three test cards of the KDT and total numbers of errors made during the test.

Study Procedure

Each participant completed three test sessions (**Figure 1**), in which they completed the KDT, over a 2-day period. Test 1 (7:00 AM Day 1) served as the baseline. Participants were instructed to avoid caffeine and sleeping during the day and to go about their normal activities. All participants returned for Test 2 at 7:00 PM on Day 1and remained in the laboratory to complete the sleep intervention. Their intervention was based on group assignments: sleep deprivation group slept approximately 8 hours while the control group slept approximately 3.5 hours. Test 3 took place on the morning of Day 2 at 7:00 AM.

Sleep Intervention

At 7:00 PM on Day 1, all participants returned to the lab and Test 2 measurements were completed. After Test 2, the participants in both groups remained in the lab to complete their respective sleep regimens: sleep deprivation group sleeping from approximately 2:30AM until

6:00AM while the control group slept from approximately 10:00PM until 6:00AM. Sleep durations were continuously monitored via ActiGraph for all participants. All participants were instructed to bring any personal items needed to spend the night in the lab, while blankets and pillows were provided. The lab located in Indiana University School of Public Health was equipped with 8 twin-sized beds and was adjacent to bathrooms, showers, and a locked room in which participants could store personal items. Participants were able to engage in sedentary activity (reading, playing video games or board games, watching movies, light walking in the lab) until their designated sleep time. Participants were provided snacks and had access to water *ad libitum*. An experimenter stayed with participants between 8:00 PM and their designated sleep time to ensure wakefulness and assist in any adverse events. At the designated sleep time the experimenter instructed participants they could sleep until 6:00 AM. At 6:00 AM, an experimenter woke participants and provided a breakfast of bagels and cream cheese. Participants were given time to wake up, complete morning routines, and prepare for Test 3. During this time, caffeinated drinks remained prohibited. Subjects in both groups completed Test 3 at 7:00 AM.

Instrumentation

Found to have a test-retest reliability of 0.89-0.97[18-20], the KDT was used to quantify saccadic velocity of ocular-motor function[7, 9, 19] and neurocognitive function. Participants were seated in a well-lit room. The KDT was administered on a hand-held tablet which the participant rested flat on the table or held in his/her hands supported by resting forearms or elbows on the table. The participant was asked to read aloud, left to right and top to bottom, a series of numbers on the test cards and to refrain from using his/her fingers as a reading guide. Guiding the participant's eyes from one number to the next, arrows on the demonstration card familiarized the participant with the test. The demonstration card was followed by the three test cards.[9] As the cards

progressed, the difficulty increased with guiding lines disappearing and numbers becoming denser. Both time and errors were recorded individually for each test and cumulatively by the experimenter. To mitigate a potential learning curve[7], three different card series were used during the three different test sessions.

Statistical Analysis

Data Processing

Statistical analyses were performed using SPSS software (IBM Corporation, Armonk, NY). Coding was used to identify the subject group placement (0=control, 1=Sleep Deprivation).

Statistical Analysis

Data exploration showed population (*N*), mean values, skewedness, distribution, and outliers. A two-way repeated measures analysis of variance (RMANOVA) was used to determine if there was significance of data points from two groups at the three time points. The RMANOVA was completed for examination of time and errors individually. A Bonferroni correction was applied to post-hoc testing to determine between which of the time points significant difference was evident. Both tests were completed to examine between group interaction and within-group interaction. A decrease in performance time demonstrates a bettered or faster performance whereas an increase of time exemplifies worsened performance.

RESULTS

A total of 198 individuals responded to recruitment emails and fliers of which 42 subjects (20 control, 22 sleep deprivation) completed testing and proceeded to statistical analysis. Refer to **Figure 2** for a delineation of exclusion. For demographic information for both groups, please refer to **Table 1.**

The two-way RMANOVA did not reveal any significance for errors (**Figure 3**) thus post-hoc testing was not warranted. However, a significant time by group interaction ($F_{(1.689,67.552)}$=8.840, p=0.001, partial η^2=0.181) was discovered for performance time from the two-way RMANOVA. Additionally, an overall significant main effect for time was revealed for the KDT performance ($F_{(1.689,67.552)}$=12.736, p<0.001, partial η^2=0.242). . **Figure 4** illustrates the average performance for each group at all three time points. Bonferroni post-hoc testing revealed that from Test 1 (41.3±5.8 seconds) to Test 2 (38.7±6.0 seconds) the sleep deprivation group improved significantly (Difference 2.6 (95%CI, 1.115 to 4.130) seconds, p<0.001). However, the sleep deprivation between Test 2 and Test 3 significantly perturbed performance in the sleep deprivation group from Test 2 to Test 3 (40.9±7.3 seconds, Difference -2.2 (95%CI, -3.677 to -0.678) seconds, p=0.002). This resulted in there being no significant 24-hour difference (Difference 0.4 (95%CI, -1.583 to 2.474) seconds, p=1.000) between Test 1 (7:00AM Day 1) and Test 3 (7:00AM Day 2) in the sleep deprivation group (**Figure 5**).

According to the Bonferroni post-hoc testing after the two-way RMANOVA, from Test 1 (42.0±4.4 seconds) to Test 2 (40.2±4.2 seconds), the control group significantly improved performance (Difference 1.9 (95%CI, 0.309 to 3.471) seconds, p=0.014). Further improvements were seen after sleeping normally between Test 2 and Test 3 (38.4±4.2 seconds, Difference 1.7 (95%CI, 0.142 to 3.288) seconds, p=0.028). These continuous improvements resulted in an overall bettered performance of 3.6 (95%CI, 1.478 to 5.732) seconds from Time 1 to Time 3 in the control group (p<0.001, **Figure 5**).

While there was a main effect for time in each group, there was no statistical difference between the groups at any time point. At Test 1, there was a 0.7 (95%CI, -2.511 to 3.965) second difference between the control group and the sleep deprivation group (p=0.653). A 1.5 (95%CI, -

1.782 to 4.701) second difference (p=0.368) was found at Test 2 between the groups (p=0.368) and at Test 3, there was a 2.4 (95%CI, -1.324 to 6.190) second difference between groups (p=0.198). **Figure 6** displays the learning effect seen in both groups without intervention while **Figure 7** illustrates the perturbed learning effect seen in the sleep deprivation group after sleep intervention.

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DISCUSSION

In the present study, the effect of partial sleep deprivation on neuro-ophthalmologic function was measured by KDT. There are two chief findings from this study: 1) restricting sleep to 3.5-hours significantly worsened performance compared to measurements before sleep intervention (Test 3 and 2) there was a considerable learning effect found throughout the three tests in the control group and between Test 1 and Test 2 in the sleep deprivation group. This is, to our knowledge, a first report demonstrating that the acute partial sleep deprivation in a laboratory setting resulted in significant perturbation in neuro-ophthalmologic circuit as measured by KDT.

The results are in alignment with a previous study in medical residencies.[21] Thirty-five neurology residents were grouped based on their status of on-call or not-on-call and completed the KDT before and after shifts. While there was no difference in sleep amounts prior to the baseline test, before the follow-up test those who were on-call reported sleeping an average of 2-hours and those who were not-on-call slept an average of 6.75-hours. These differences in sleep duration manifested a decline in ocular-motor function, where those who were not-on-call improved their tests performance significantly by 3.8 seconds compared to those on-call who had a worsened performance of 0.23 seconds. Comparatively, the present study found a similar improvement in the control group and much more robust deterioration of the sleep deprived group with an addition of 2.2 seconds after the sleep intervention. Furthermore, both the resident study and the study at hand found errors to be randomly made by individuals throughout both groups and were clinically meaningless for detecting the effect of sleep deprivation. Unlike the aforementioned clinical study, the current study was well-controlled, revealing true sleep deprivation effects. We regulated subjects to sleep ample duration (7h or more) for 7 days leading up to the study and restricted caffeine and alcohol intake, while medical residents were allowed to consume unlimited amounts of caffeine. Nonetheless, the present study supports the previous study by demonstrating acute sleep deprivation negatively effects KDT performance and blunts learning effects.

Due to the KDT's reliance of saccadic movement, the worsened performance is parallel with other research examining the reaction of saccadic velocity after various amounts of sleep deprivation.[6, 22, 23] For example, in thirteen participants with the average age of 24 years old, Goldich et al. found that 24-, 26-, and 28-hours of sleep restriction led to a worsening of eight percent in velocity of saccadic movements.[24] Additionally, significant decrease in saccadic velocity was found in participants with partial sleep deprivation (4h night sleep) for a night

followed by sleep deprivation for 64 hours.[6] Interestingly, the ocular-motor perturbation induced by sleep deprivation did not correlate to the sleepiness reported by the subject.[23]

Beyond saccadic perturbations, the neurocognitive aspect of the KDT may have been negatively impacted by the sleep intervention adding to the worsened performance. Since completion of KDT involves sight, processing, motor function, and speech, the brain at the brainstem, cerebellum, and cerebral cortex must be engaged in order for proper completion of the task. A deterioration of these structures has been measured in a chronic sleep deprivation study by Van Dongen et al.[25] in which participants slept 8-, 6-, or 4-hours per night for 14 days or completely sleep deprived for 3 days. Intermitted measurements taken in form of psychomotor vigilance task, computerized digit symbol matching task, and serial addition/subtraction resulted in dose-dependent deficits in all tasks in all groups.[25] When compared to the acute sleep deprivation, those that slept less than 6 hours for 14 days were equally disturbed in alertness and working memory as those in after one night of complete sleep deprivation concluding that neurobehavior and neurocognitive function are negatively affected by both acute and chronic sleep restriction.[25]

Multiple studies[19, 20] have concluded that the KDT is a reliable tool to reflect neurotrauma induced by mechanical force. Ample studies[7, 9, 16, 20, 26] report that KD performance can be worsen by 14% and as much as 300% from baseline levels by brain trauma. However, none of these studies accounted for the sleep duration when administering the KDT, which may lead to significant falsified testing. The KDT has a reported minimal detectable change of 5.9 seconds to assess for a concussion.[27] Baseline testing completed in a sleep deprived state will not be accurate and may lead to a false negative diagnosis when compared to a post-injury test. Contrarily, if the post-injury

test is completed in a sleep deprived state, the increased time may be falsely attributed to a concussion when, in fact, it is due to sleep deprivation.

Furthermore, while the learning effect seen in the present study may have been exaggerated due to the proximity of the tests within the 24-hour period, the finding has also been seen in other studies examining the KDT.[8, 26, 28] The significant improvement of performance over multiple baseline tests in the control group is noteworthy for clinicians using the test as a concussion assessment tool. If a participant's baseline performance is not consistent within the same day, then a clinician should be cautious to rely on a post-injury comparison to the changing baseline for concussion assessment. Multiple same-day administrations of the KDT baseline measures is warranted to account for the learning effect. This is supported on the KDT website instructing a baseline test be conducted twice and the better performance should stand as the true baseline. Future research is needed to fully understand after how many administrations does the performance stabilize.

Limitations

The participants only slept in the sleep laboratory during the time of the sleep intervention. Prior sleep deprivation research[4] allowed participants to have adjustment periods during which they would sleep normally in the sleep lab familiarizing themselves to the environment. While not having the adjustment period did not seem to significantly alter the quantity of sleep of participants, it may have affected their quality of sleep. Overall, this study did not examine quality of sleep rather the average sleep durations.

While this study examined acute sleep deprivation, future research should examine the effects of chronic sleep deprivation on KDT performance due to the prevalence of sleep deprivation.[1-3] Sleep deprivation's impact on the measurements of other concussion assessment

tools like the ImPACT Test and SCAT5 should be evaluated in case of other falsification of baseline or post-injury testing results.

Conclusions

Sleep deprivation negatively effects neurocognitive and ocular-motor function as assed by the KDT. As a widely used concussion evaluation tool, understanding sleep deprivation's impact on KDT performance is crucial for clinicians in order to assess for concussion. Sleep durations, especially if less than 7 hours per night, should be an important part of interpreting results of the KDT at baseline and at post-injury to avoid false determinations. To correct for the observed learning effect, multiple administrations of the KDT should take place.

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TABLE AND FIGURE LEGENDS

Table 1. Demographic Information. The breakdown of sex, age, height, weight, and sleep amounts per group. Only the quantity of sleep during the sleep intervention was significant between groups, which was controlled for as the sleep deprivation group was only allowed to sleep 3.5 hours while the control group could sleep 8 hours.

Figure 1. Study Design. Participants in both the sleep deprivation group and control group received a sleep log and activity monitor one week prior to Test 1. They completed Test 1-3 at the respective time points. The sleep intervention took place between Test 2 and Test 3. During this time, the sleep deprivation group slept only 3.5 hours, while the control group slept 8 hours.

Figure 2. Participant Delineation. Of 198 individuals who reached out in interest, only 42 completed the study. This illustrates the stages of voluntary dropouts and study exclusions.

Figure 3. Repeated Measures Analysis of Variance Errors. Errors did not have a time by group interaction nor a main effect for time. Further, small observed power indicates that the number of errors made by participants was unaffected by time of day and sleep intervention.

Figure 4. Overall. There was no difference between the groups at any of the three Test sessions. However, this figure illustrates how the sleep deprivation negatively impacted the sleep deprivation group compared to the control group. Both groups improved from Test 1 at 7am to Test 2 at 7pm. From Test 2 to Test 3, both groups were subjected to sleep interventions. The control group was allowed to sleep 8-hours and continued to improve their performance while the sleep deprivation group worsen performance time after 3.5 hours of sleep.

Figure 5. 24-Hour Difference. The control group showed overall improvement from Test 1 at 7am on Day 1 to Test 3 at 7am on Day 2. Contrarily, the sleep deprivation group did not improve significantly from Test 1 to Test 3 due to the perturbation of sleep restriction.

Figure 6. Sleep Deprivation Effect. The learning effect is reversed with sleep restriction at the sleep intervention.

Figure 7. Learning Effect. Without any intervention, both groups performed better after the initial test.

TABLES

Table 1. Demographics Information

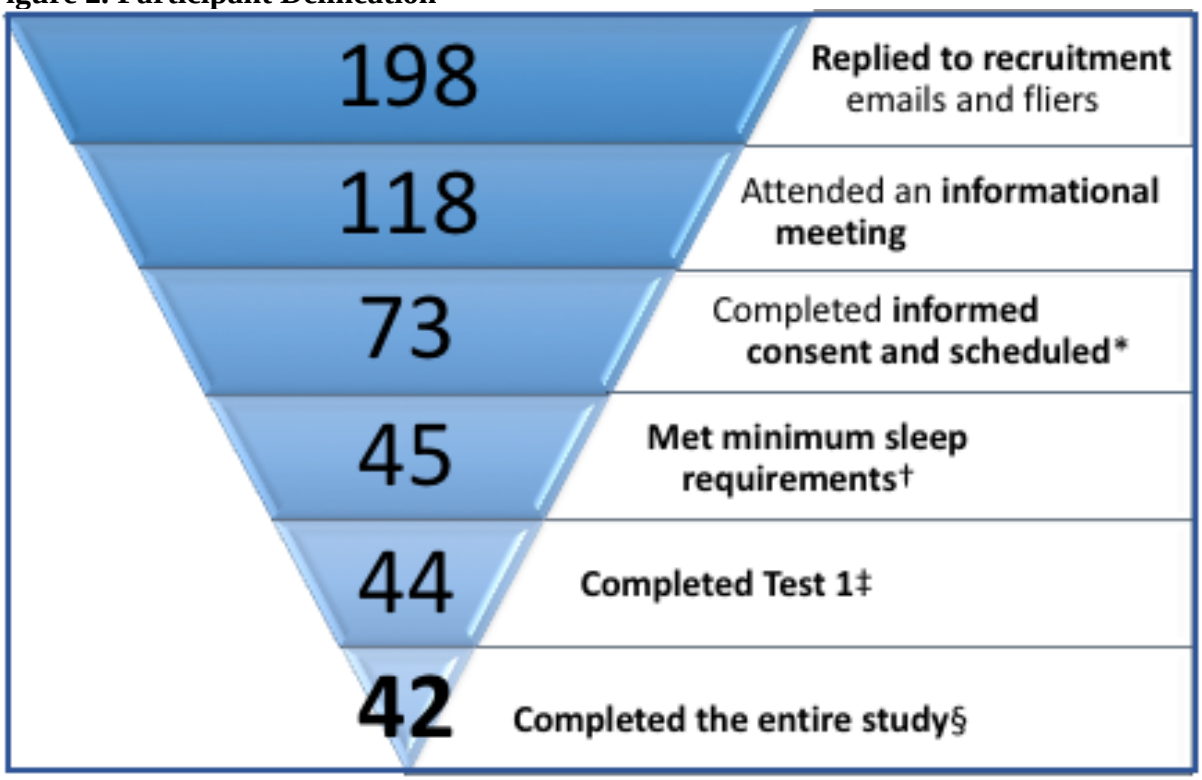
	Control Group	Sleep Deprivation Group	P-Value
Sex	11F, 9M	12M, 10F	
Age	20.6±1.2	20.6±1.4	0.830
Height (cm)	166.3±12.5	173.2±9.7	0.054
Mass (kg)	67.0±10.5	73.9±13.4	0.072
Average Sleep Prior to Study (min)	453.4±34.0	439.4±44.9	0.266
Sleep Intervention (min)	419.7±33.6	188.3±29.6	<0.001

FIGURES

Figure 1. Study Design

Group	1 Week Prior Activity Graph & Sleep Log	Day 1		Sleep Intervention	Day 2
		Test 1 7:00 AM	Test 2 7:00 PM		Test 3 7:00 AM
Control	✔	✔	✔	8 hours	✔
Sleep Deprivation	✔	✔	✔	3.5 hours	✔

Figure 2. Participant Delineation



* 38 chose not to complete informed consent due to lack or interest or not meeting inclusion criteria; 7 completed informed consent but did not schedule

† 26 did not meet minimum average sleep requirements; 2 technology failures which did not objectively record sleep

‡1 did not show up

§1 asked to reschedule after Test 1; 1 voluntarily withdrew between Test 2 and Test 3

Figure 3. Repeated Measures Analysis of Variance Errors

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[a]
Time	Sphericity Assumed	.393	2	.197	.450	.639	.011	.901	.121
	Greenhouse-Geisser	.393	1.503	.262	.450	.584	.011	.677	.111
	Huynh-Feldt	.393	1.587	.248	.450	.594	.011	.715	.113
	Lower-bound	.393	1.000	.393	.450	.506	.011	.450	.100
Time * SleepDep1yes0no	Sphericity Assumed	1.981	2	.990	2.268	.110	.054	4.537	.449
	Greenhouse-Geisser	1.981	1.503	1.318	2.268	.125	.054	3.408	.384
	Huynh-Feldt	1.981	1.587	1.248	2.268	.123	.054	3.601	.396
	Lower-bound	1.981	1.000	1.981	2.268	.140	.054	2.268	.312
Error(Time)	Sphericity Assumed	34.924	80	.437					
	Greenhouse-Geisser	34.924	60.101	.581					
	Huynh-Feldt	34.924	63.491	.550					
	Lower-bound	34.924	40.000	.873					

a. Computed using alpha = .05

Figure 4. Group Differences Overall.

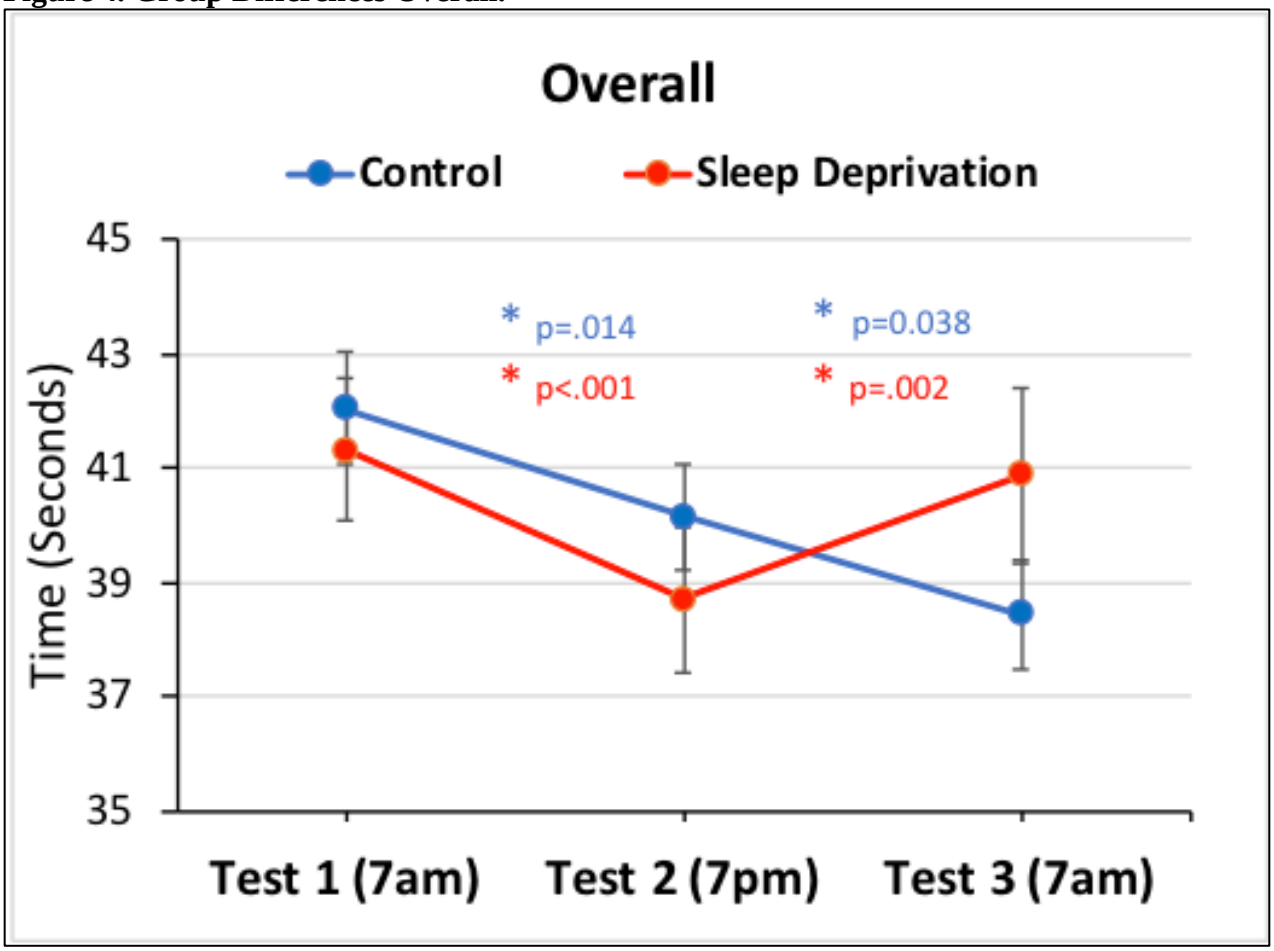


Figure 5. 24-Hours Difference

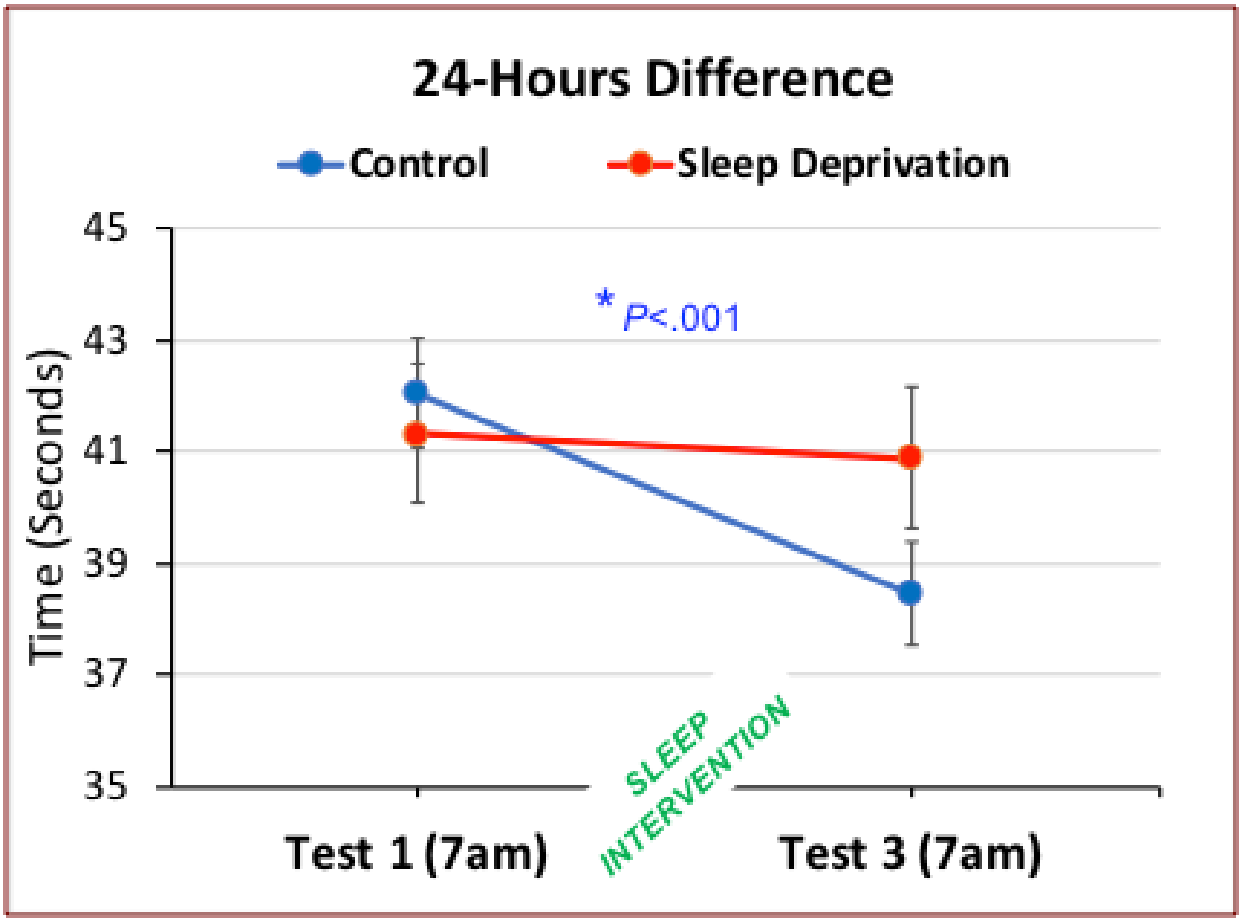


Figure 6. Sleep Deprivation Effect

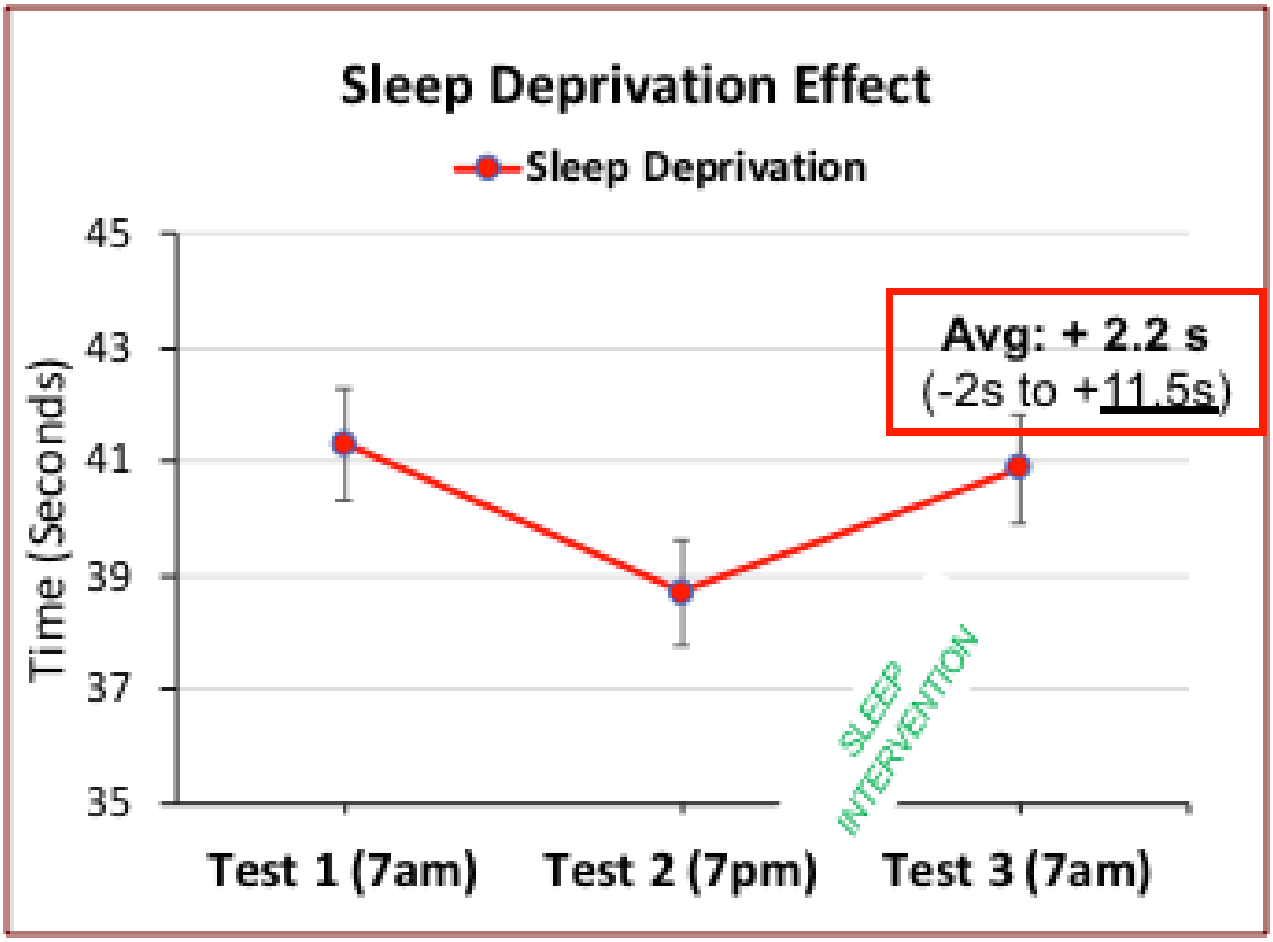


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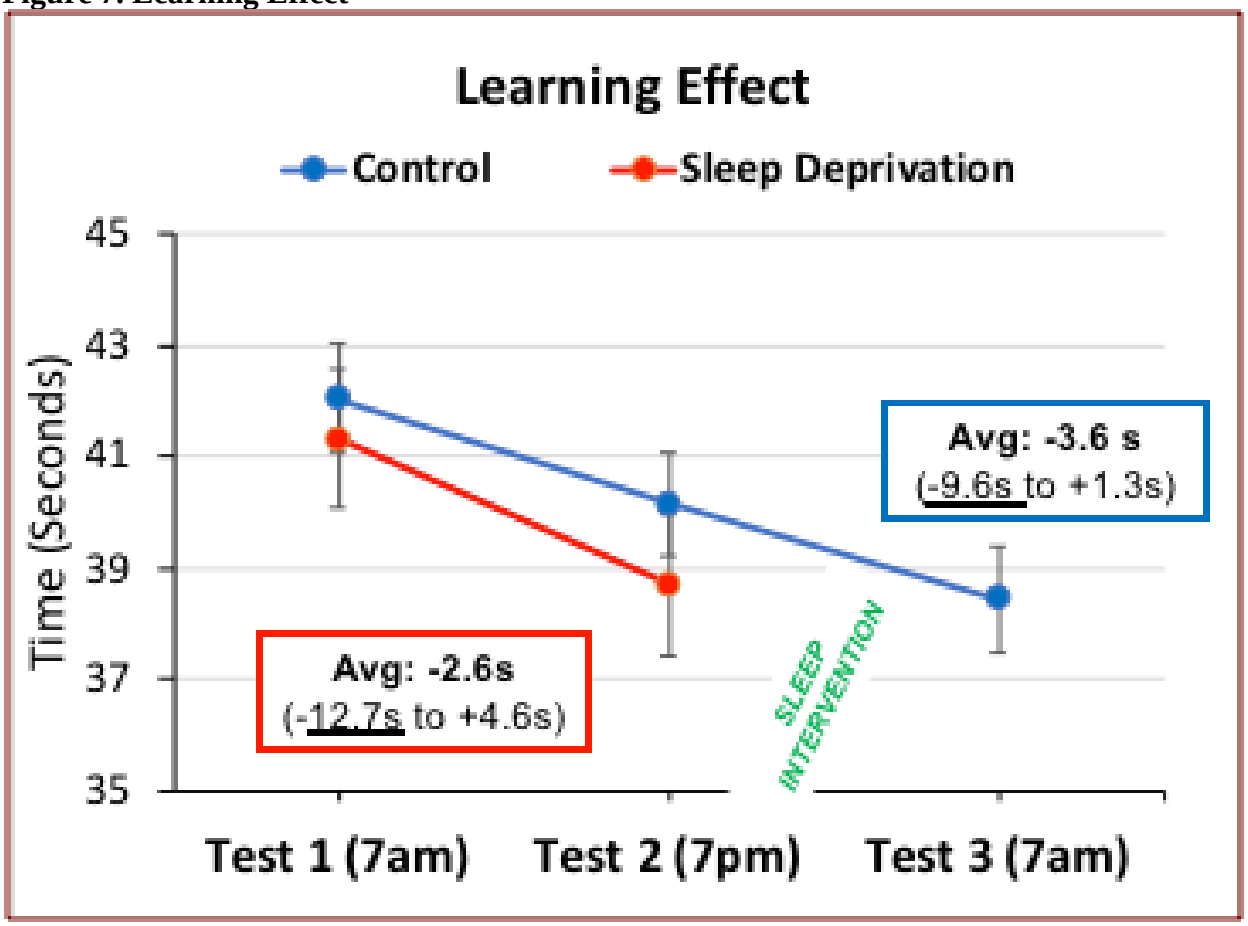
Figure 7. Learning Effect



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APPENDICIES

APPENDIX A:

Operational Definitions, Limitations, Assumptions, Delimitations, Statement of the Problem, Purpose Statement

OPERATIONAL DEFINITIONS

Near Point of Convergence – The near point of convergence is the closest point at which an individual can focus clearly on an object directly in his/her line of vision. Both eyes must be adducted by the median rectus muscle innervated by the oculomotor nerve (Cranial Nerve III).

Partial Sleep Deprivation – The restriction of sleep to be less than the recommended amount of 7 to 9 hours of sleep per night. Unlike total sleep deprivation, partial sleep deprivation is not an entire lack of sleep. In this study, participants are allowed four hours of sleep in fulfillment of partial sleep deprivation.

Saccades – Controlled by lateral and medial rectus muscles, saccades are lateral eye movements that allow the eye to change focus from one object to the next accurately and precisely.[1-4]

Smooth Pursuits – Smooth pursuits are the eye's ability to track a moving object. This involves using sensory feedback to predict the targets trajectory.[1,3,5]

Subconcussion – Subconcussion is a low-magnitude head impact that does not result in clinical symptoms and thus, is often over looked in research.

ASSUMPTIONS

The following assumptions apply to this study:

1. Soccer players have proficient and similar soccer heading technique and experience which minimizes the variation of head impact between the subconcussive impact group and the sleep deprivation with subconcussive impact group participants.
2. Participants are truthful in their accounts of medical history, soccer participation and soccer heading experience, and normal sleep patterns.
3. Participants are representative of other similarly experienced soccer players.
4. Participants have similar dietary habits as they are in similar socioeconomic statuses

5. Participants obey instruction not to sleep during the day nor to consume caffeinated beverages.
6. Data collected from the EYE-SYNC Headset and the Triax accelerometer is accurate and reliable.

DELIMITATIONS

The following delimitations apply to this study:

1. Participants are active soccer players with at least 5 years of soccer heading experience.
2. Participants will be young adults, ages 18 to 26 years of age.
3. Participants have normal or corrected-to-normal vision. Participants may use contacts to correct vision, however, glasses are prohibited.
4. Participants sleep the recommended 7-9 hours per night.
5. Participants do not have any history of vestibular, ocular, or vision dysfunctions nor have any neurological or sleep disorders.
6. Participants do not have a medical prescription of caffeine.
7. Participants have not had any head, neck, or face injury in the six months prior to the study nor have they had any severe injury to the bones, joints, or muscles in either arm.
8. Ocular-motor measurements will be collected in the same location each Test session.
9. Data collection will begin with the ActiGraph bracelet one week prior to the baseline test (Test 1).
10. Data collection will continue with three subsequent testing sessions.
11. Participants in the sleep deprivation protocol will be monitored from 08.00 Day 1 to 03.00 Day 2 to ensure wakefulness.

LIMITATIONS

The following limitations will apply to this study:

1. The current study only includes soccer players, yielding less ability to generalize results to other sports
2. We only include college-aged participants, which narrowed clinical implication in different generations.
3. We will not be able to monitor subjects' activity during the day (between Test 1 and Test 2), therefore, we cannot restrict their activity levels. However, the subjects' activity levels are measured via ActiGraph wrist-based activity tracker.
4. Beyond restricted caffeine consumption, the subjects do not have dietary regimen, which may render varying energy levels between subjects.
5. Subjects are partially sleep deprived, which may decrease the impact of sleep depravity on ocular-motor function compared to total sleep deprivation.
6. There is no period for the subjects to adjust to sleeping in a lab during the night of sleep deprivation, which may decrease the quality of sleep.
7. Sleep quality is not objectively measured during the partial sleep deprivation protocol, yielding potential unknown variation of sleep quality between participants.
8. There may be a learning curve to the ocular-motor assessments.

STATEMENT OF THE PROBLEM

Sleep deprivation is prevalent in students in the United States. Likewise, subconcussive impacts are ubiquitous in contact sports such as American football and soccer. To the best of our knowledge there is no current research examining the individual effects of subconcussive impacts on the saccades and smooth pursuit aspects of ocular-motor function, nor is there research

examining the combined effects of sleep deprivation and subconcussive impacts. The purpose of this study is to fill this knowledge gap and examine the acute combined effects of sleep deprivation with subconcussive impacts on ocular-motor function. The central hypothesis of this study is that sleep deprivation may have a negative impact on ocular-motor function and therefore may worsen the ocular-motor function measured after subconcussive impacts.

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APPENDIX B:

REVIEW OF LITERATURE

INTRODUCTION

Ocular-motor function can be measured by quantifying the succession and efficiency of eye movements including saccades, smooth pursuits, and convergence. These measurements allow researchers to delineate how the brain is functioning since approximately half of the brain's circuits are related to vision and ocular-motor function.[1] Consequently, when the brain is not preforming in an optimal state, abnormalities in ocular-motor function may be observed. Situations in which the brain may not function normally include in a state of sleep deprivation. The King-Devick Test, a sideline concussion assessment tool, relies on both saccadic and convergence function and may be able to detect abnormalities in ocular-motor function due to sleep deprivation. This review of literature outlines what is currently known of the effects of sleep deprivation on ocular-motor function and the use of King-Devick Test for ocular-motor assessment.

Ocular-Motor Measurements

Vision and ocular-motor functions are linked to multiple aspects of brain function, including that of the dorsolateral prefrontal cortex, and have been identified as a practical and reliable means of assessing brain function.[1-3] Several functions of the ocular-motor system have

Table 1. Ocular-motor based function, description, and method of assessment*

Visual function	Description	Method of Assessment
Pursuit	Following a moving object using received information and creating a predictive trajectory	Vestibulo-Ocular Motor Screening; Eye tracker; optometrist
Saccades	Fast eye movements to accurately and precisely change focus from one object of interest to another	King-Devick Test; Eye tracker; optometrist
Convergence	Ability move eyes simultaneously in opposite horizontal directions to follow an object as in moves toward oneself	Near-Point of Convergence Beren's Ruler; Optometrist

*adapted from Ventura et al.[3] and Hunt et al.[8]

been identified as vulnerable to impairment from injury.[4-6] In particular, saccades, smooth pursuit, and near point convergence have been well-studied, given their sensitivity to various types and severity of neuronal defect. Furthermore, recent technological advancement enables researchers and clinicians to objectively and reliably measuring the function of the ocular-motor system (Table 1).[1, 2, 7, 8]

Saccades

Saccades are rapid movements of the eye from one object of interest to another with precision, accuracy, and anticipation.[2, 6, 9, 10] Neurologically, saccades are chiefly controlled by the cranial nerves: oculomotor (III), trochlear (IV), and abducens (VI), with accessory information derived from the basal ganglia, frontal lobe, and cerebellum of the brain.[7, 11] Most dominant muscular control of the eye for saccades comes from the lateral rectus muscle. Saccadic eye movements are often measured in the form of a velocity, spatial acceleration, and accuracy. Different types of saccades are voluntary, which can be tested with the King-Devick Test, and reflexive, an involuntary response to a sudden appearance of an object in the field of vision.[10] Voluntary saccades are made with the intention of a goal.[10]

Smooth Pursuit

Pursuits are eye movements that allow individuals to successfully follow and focus on a moving object.[2, 7, 9] Smooth pursuits are pursuits in which the velocity of the moving object match that of eye's pursuit, which requires a balance of feedback and prediction of movement pattern.[2, 6, 7, 9] The received feedback reflects on the retina as a new image every time the object is in a new position in space, which then allows the eye to predict where the object's trajectory.[2, 6]

Most frequently, smooth pursuits are measured in conjunction with saccades by an eye tracker; this combination of smooth pursuits and saccades is known as visual tracking.[2, 11] Visual tracking requires attention, prediction, and smooth pursuit of the target (see **Figure 1, Figure 2**). The subject watches a target moving through a set pattern on a computer screen and video-oculography methods and records how successfully

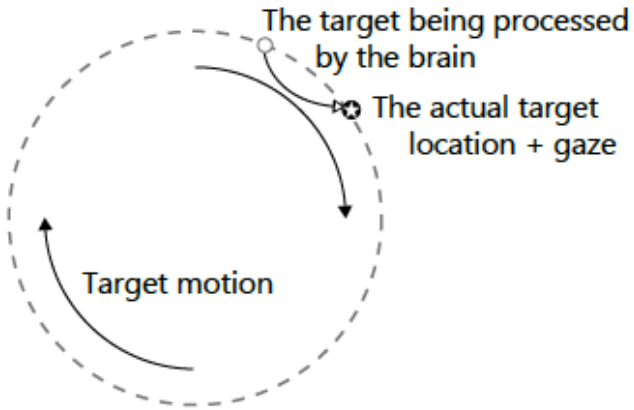

Figure 1. Prediction of target motion. Prediction and visulomotor synchronization. Maintaining the gaze on the target requires synchronization of the motor output with predicted target motion, rather than the incoming sensory information. Reproduced from Maruta and Ghajar.[12]

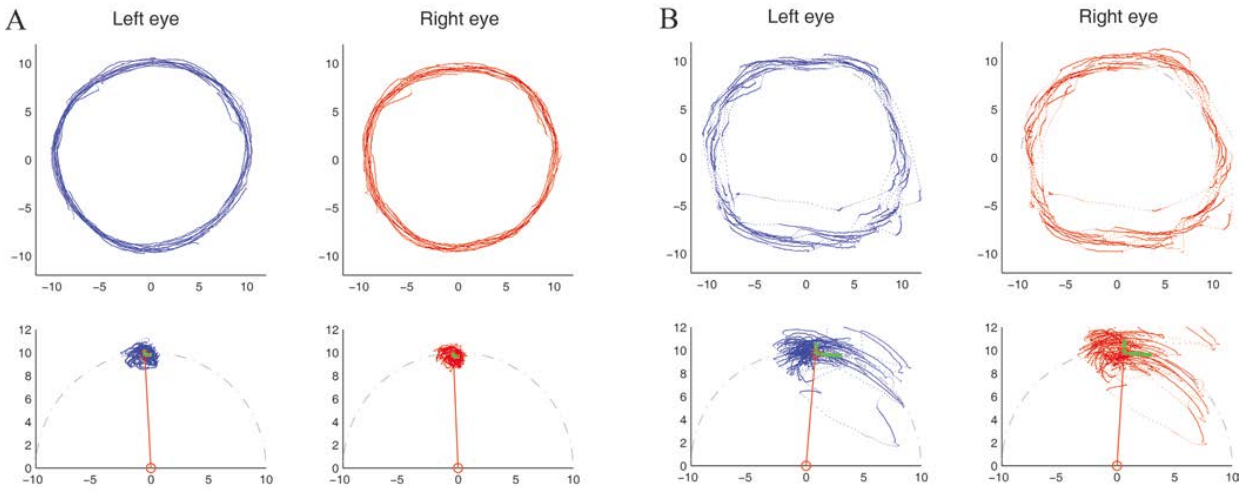

Figure 2. Representative scattergrams of gaze positions (blue indicates left eye, and red indicates right eye) relative to the target; gaze positions were gathered at a frequency of 500 Hz. Circular patterns represent the path of the eye following a dot moving in a circle, and the semicircular pattern represents the eye position versus the target. Deviation from a target trajectory (dashed line) in both normal (A) and postconcussive (B) patients. A concussion signal is indicated by eye positions jumping ahead of the dot shown in B and C. Reproduced from Sussman et al.[2]

and smoothly the subject is able to follow the target.[2] The consistent radius of a circle and velocity of the target allows predictable target trajectory.[11, 12]

Near-point of Convergence

Convergence is the abduction of both eyes by medial rectus muscles to focus on an object in a subject's proximal field of vision.[5] Near-point of convergence is the point at which an individual can focus on an object before diplopia occurs.[13] Although no normative value for a specific demographic has been determined, the average near point convergence of subjects ages 18-22 years old is between 5-8cm.[5, 13-15] Abnormalities in an individual's ability to converge can elicit headache, difficulty reading, difficulty focusing, and blurred vision.[5]

Sleep Deprivation

While there is a developmental pattern related to sleep duration, the optimal number of hours of sleep for adolescents in the United States is greater than or equal to nine hours per night.[16, 17] Multiple studies found that only 7.6% of high school students nationally are meeting this ideal sleep goal.[16, 18] In fact, by interviewing 3476 students in 8th grade and 10th grade, Paiva and colleagues found that as students, regardless of sex, progress through high school their sleep deprivation worsens.[17, 18] Researchers attribute the prevalent sleep deprivation to varying biological and social factors, including employment status, social interaction, caffeine consumption, and age or stage of life.[16, 17] The causes of sleep deprivation vastly vary, however, it is assured that without sleep one can expect to experience detrimental side effects to both mental and physical health. Contrarily, the benefits of prolonged sleep and sleep banking are emerging in recent research. Regardless of the cause, limited sleep warrants adverse symptoms that are similar to concussion: headache, fatigue, depressed mood, and difficulty concentrating.[16, 19] Furthermore, there are health risks that are associated with chronic sleep deprivation such as

diabetes, hypertension, and obesity amongst others.[17] Beyond altered emotional and health statuses, sleep deprivation causes decreased alertness, reaction times, and cognitive function.[20, 21]

To understand the effects of sleep deprivation and mood, Short et al.[19] recruited twelve healthy high school students ages 14-18 years old to complete the Short Form of Profile of Mood States every two hours while awake. Baseline moods were compared to the mood following one night of complete sleep deprivation. The results showed that, throughout the day following sleep deprivation, there was a significant increase in depressive mood, confusion, anxiety, anger, and fatigue while vigor significantly decreased.[19] Interestingly, the study revealed that there may be differences in mood reaction between the sexes with females and males expressing significantly more anxiety and less vigor, respectively.[19] Additionally, emotional empathy may be negatively affected by sleep deprivation. Exploration of this proposed decay of emotional empathy was the purpose of a study designed by Guadagni et al.[22] in which thirty-seven healthy individuals were subjected to the Multifaceted Empathy Test before and after a sleep intervention. Participants who experience total sleep deprivation were found to have hyposensitivity to others' direct and indirect emotions when compared to participants who slept a full night.[22] The diminished ability to understand others' emotions directly impacts the quality of one's social relationships and interactions.

While mood and emotional empathy deteriorate with sleep deprivation, sensitivity to pain may increase in such a state. A meta-analysis conducted by Schrimpf et al. concluded that pain perception was moderately affected by sleep deprivation in between-group analysis and a largely effect when examining within-group analysis.[23] This lower tolerance to pain may be a result of the surplus of negative emotions in subjects following sleep deprivation. Individuals

experiencing pain may have a decreased quality of life, which may lead to further health conditions.

Interestingly, in addition to acute effects of sleep deprivation, multiple reviews have concluded that not only are there detrimental health effects of sleep deprivation, that in fact, over time, there are also similar effects for individuals who sleep for consistently long periods of time. These summaries are quite controversial as the relative risk varies between studies from low to moderate. However, there is consistent evidence that both sleep deprivation and elongated sleep over several years may lead to increased all-cause mortality, cardiovascular disease, and symptomatic diabetes.[24, 25] After performing a meta-analysis of twenty-three prospective cohort studies in 2009, Gallicchio and colleagues found that the all-cause mortality rate is significantly associated with short- and long-term sleep durations with medium sleep amount equating 7-7.9 hours/night. Explaining this two way phenomenon are the characteristics of both long- and short-duration sleepers. For example, those who sleep less than 7 hours or more than 8 hours per night regularly may be unhealthy due to other outstanding conditions such as lower income, increased depression, and decreased activity level.[25]

Despite the controversial fatal effects of chronic sleep extension, there are several studies that promote sleep extension as a method to improve vigilance and athletic performance compared to habitual sleep patterns.[26, 27] First, sleep extension or sleep banking prior to sleep deprivation has been found to reduce the negative side effects of sleep deprivation as concluded by Arnal et al.[26] For six nights in a row fourteen healthy male participants slept either habitually or in extended states prior to undergoing one night of total sleep deprivation in a study designed by. At baseline, after sleep deprivation, and after one night of recovery sleep, measurements were taken of participants' Psychomotor Vigilance Task Performance. Those in the sleep

extension group prior to the night of sleep deprivation performed faster and with fewer errors than participants who slept habitually prior to the night of total sleep deprivation. Further, those who "banked" their sleep, recovered from the sleep deprived night faster than those who did not have extended sleep.[26]

To exemplify the benefits to prolonged sleep periods on athletic performance, Mah et al. monitored the sleep patterned of eleven members of the Stanford University varsity men's basketball team. During pre-season, the participants slept in their normal routine, obtaining six to nine hours of sleep per night. During season and as intervention in the study, participants slept a minimum of 10 hours per night. Shooting accuracy, sprint times, and participants' ratings of personal physical and mental well-being improved as they sleep quantity increased pre-season to in-season.[27] The study concluded that achieving optimal amounts of sleep may improve athletic performance.[27]

Another sleep extension study examined fifteen healthy undergraduate students' alertness, reaction times, and mood.[28] Participants' regular sleep quantities, averaging approximately seven hours per night, were taken over a seven-day period followed by baseline testing. After participants slept limitlessly, average of 9.4 hours of sleep per night, for a seven-night period, re-testing was completed. A final test was administered at the end of the study, when the participant could no longer obtain limitless sleep due to schedule conflicts, or when the test results displayed maximal alertness levels. The study concluded that limitless sleep significantly improved reaction time, daytime alertness, and mood compared to baseline testing.[28]

Sleep quantity and quality can be measured using an array of tools and equipment. However, ocular-motor function measurements allow insight into neurocognitive function and may be able to objectively identify diverse effects of sleep deprivation.

Effects of Sleep Deprivation on Ocular-Motor Function

Lack of sleep is known to trigger various sensory perturbations (e.g., vestibular, ocular-motor, tactile, and pain). Emerging evidence suggests that the eye movement paradigm is particularly susceptible to sleep deprivation, suggested by compelling studies examining the immediate effects of sleep restriction by measuring saccadic velocity, eyelid blinking rate, pupil constriction.[29] Simultaneously, the efficiency of a recovery from sleep deprivation has been largely investigated to answer a question: how long does it take to normalize to the individual's baseline? In this context, the relationship between sleep and ocular-motor function will be appraised to evaluate the effects of sleep quality on ocular-motor system.[21, 30]

Experiments examining saccadic velocity did so with variations of sleep depravity. In thirteen participants with the average age of 24 years old, Goldich et al. found that 24, 26, and 28 hours of sleep restriction led to a decrease of eight percent in velocity of saccadic movements.[31] It is worthy to note that Goldich et al. did not find significant difference in pupillary diameter and constriction amplitude. The linkage between sleep restriction and decreased saccadic velocity was corroborated by other researchers.[21, 30, 32] For example, after a period of normal sleep, the participants in Rowland et al.'s study were allowed to only sleep for four hours and then were totally sleep deprived for 64 hours. After the 64 continuous hours of sleep deprivation, the participants were allowed a night of 10 hours of sleep to recover. Using a polysomnography and Fitness Impairment Test, Stanford Sleepiness Scale, and a driving simulator, pupil constriction latency was significantly increased, while saccadic function was perturbed, as

illustrated by a significant decrease in saccadic velocity. Intriguingly, following 10 hour of recovery night sleep, both latency to pupil constriction and delayed saccadic velocity were normalized to baseline levels, indicating that sleep deprivation transiently impaired pupil response and saccadic eye movementy.[21] A similar study by Zils et al. revealed one night of total sleep deprivation the accuracy of prosaccades was decreased, the peak velocity of all saccades was reduced.[30] Again, there was no significant difference between the baseline measurements and the measurements taken after the night of recovery sleep.[30] While finding that sleep deprivation negatively effects the ocular-motor system, it was noted that the impacts of sleep deprivation on the ocular-motor system were not correlated to the sleepiness reported by the subject in a study completed by Fransson et al.[32]

Mixed results were found in a study by Rowland et al.: statistically significant results found in only one of four groups. Of the sleep deprivation groups (3-, 5-, 7-, and 9-hours of sleep deprivation), only the subjects of the 3-hour sleep restriction group showed statistically significant differences in pre- and post- sleep deprivation saccadic velocity measurement.[33] In all other groups, both during experimental and recovery phases, there were no statistically significant differences.[33]

Furthermore, no statistically significant variation in reaction time and velocity of the saccades pre- and post- sleep deprivation was the result of 24-hour sleep deprivation in a study done by Fimm et al.[34] In a partial sleep deprivation study by Crevits et al., no statistically significant difference between latency and number of errors of the different saccade tasks pre- and post- 20-hour sleep deprivation.[10] However, Crevits et al. found that the blinking rate was significantly higher at the end of the sleep deprivation compared to the baseline.[10] Despite there

being no statistical significance, researchers did note a trend between sleepiness and decreased peak velocity that supports the communal findings in this field of research.[34]

King-Devick Test

The King-Devick Test (**Figure 3**) has been found to be a valid and reliable test used to detect the presence of a concussion or mild traumatic brain injury.[2, 3, 35-37] The test takes approximately two minutes to complete. After completing an untimed demonstration card, the

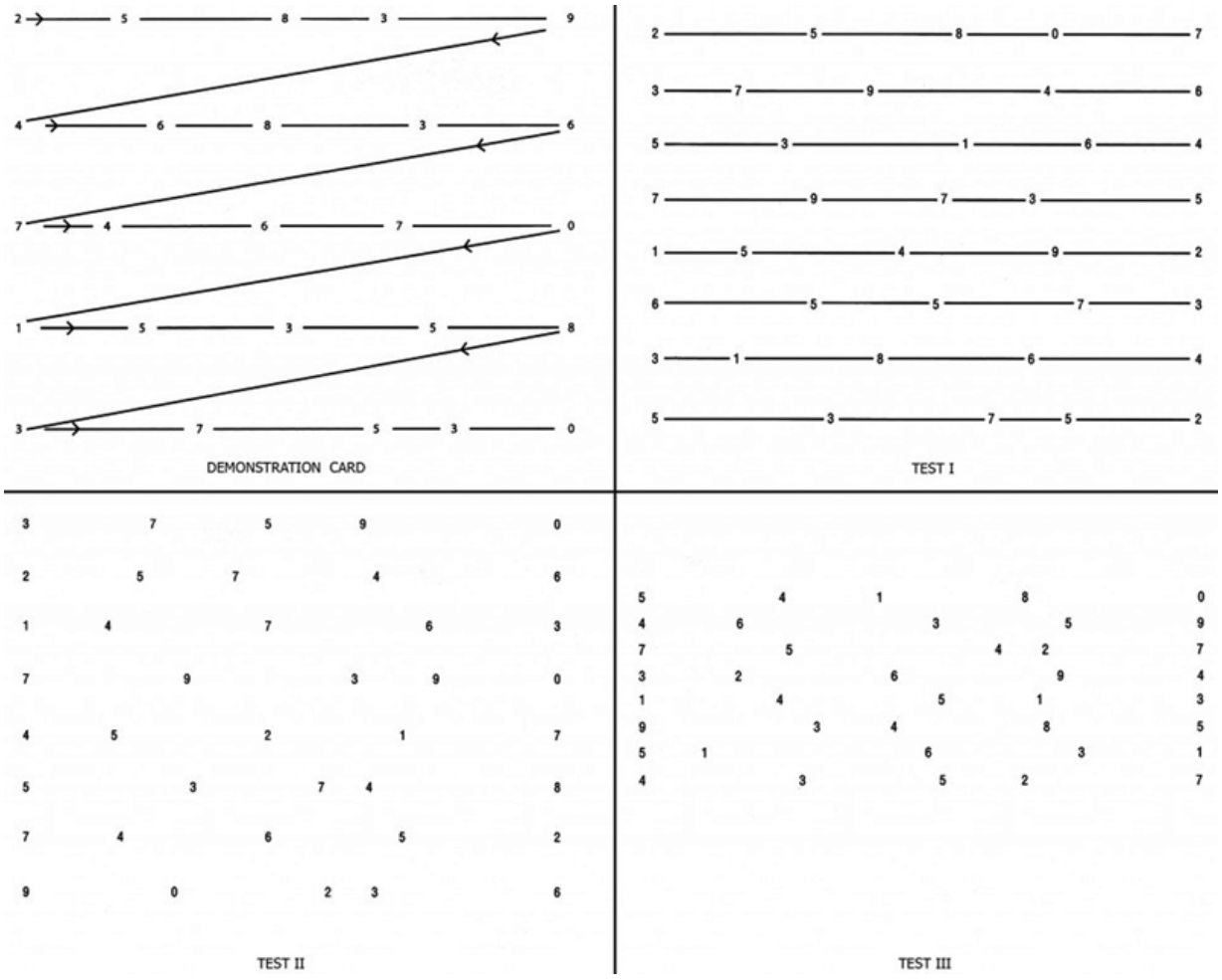

Figure 3: King-Devick Test Cards. King-Devick Test, which consists of 1 demonstration card and 3 test cards. Participants are instructed to read the numbers on each card from left to right as quickly as possible without making any errors. The sum of the time scores from all 3 test cards is the summary score or K-D time score for the entire test. The number of errors made in reading the test cards is also recorded. Reproduced from Leong et al.[37]

subject orates the numbers spread out on three cards as fast and accurately as possible. As the test cards progress from first to third, the task becomes increasingly difficult as guide lines disappear and the numbers become denser and closer in proximity. Cumulative time participants require to complete all three test cards and errors made during the testing are recorded. Between sight, processing, motor function, and speech, the brain at the brainstem, cerebellum, and cerebral cortex must be engaged in order for proper completion of the task.

A mild traumatic brain injury negatively impacts these sections of the brain. Thus, a concussion should be suspected if there is a cumulative increase in time greater than 6.10 seconds between the baseline test and the re-test or post-injury test.[38] Such a statistic is not only published by the King-Devick website, but also the result of multiple studies including one examining 157 high school athletes by Alsalaheen et al.[38] The study provides normative values for high school football players ages 13-15 and 16-18 year which contradicts the King-Devick Test instructions to compare a post-injury test to a baseline test performed by the same individual within 12-month time.[39] In fact, there are two studies that found the King-Devick Test as an unreliable tool to diagnose concussion against a normative data.[40, 41] First, emergency department physicians administered a complete SCAT2 and King-Devick Test to twenty-six individuals.[40] As a predictor of mild traumatic brain injury with no baseline comparison, King-Devick Test was not reliable compared to the results of the SCAT2.[40] The second study collected normative reference values from 158 male ice hockey players.[41] Although there were differences in age, education level, and prior concussions amongst the players, there were no distinguishable differences or have any categorical association.[41] Often times in adults without a concussion, the re-test times are reduced when compared to the individual's baseline, exemplifying a learning effect.[1, 35, 42]

One study discovered that athletes without a concussion and in a state of exertional fatigue immediately after a practice or game also demonstrate the learning effect.[35]

King-Devick Test and Ocular-Motor Function

With the saccadic eye movements combined with the cognitive function of reading numbers aloud, the King-Devick test examines the function of multiple facets of the brain including eye fields (frontal eye fields, supplementary eye fields), dorsolateral prefrontal cortex, cerebellum, cerebral cortex, and deeper structures of the brain stem.[1, 3, 36] It is noteworthy that the King- Devick Test isolates saccades as the only ocular-motor function under examination in the test due to the rapid succession of focusing on one numerical figure to the next.[5] In fact, there are a total of nearly 2,500 horizontal saccades and 371 oblique saccades are completed over the course of the King-Devick Test.[43] While it can be argued that, with the task of reading, convergence skills are additionally required, the ability to converge is scrutinized by measuring the nearest point of convergence rather than reading at a comfortable distance.

To appreciate ocular-motor function that takes place during the King-Devick Test, infrared oculography was used to track participants eye movement while completing the King-Devick Test (**Figure 4**). In this study of 67 subjects, of which 25 had experienced a chronic concussion, reading times were increased significantly in the concussion group compared to the control group.[44] This was not the credit of saccadic velocity as it was found to be similar between the groups. Rather the deterioration of performance can be attributed to the increase of intersaccadic interval, or the time between the number-to-number saccadic movement, which increased in the chronically concussed subjects compared to the healthy controls.[44]

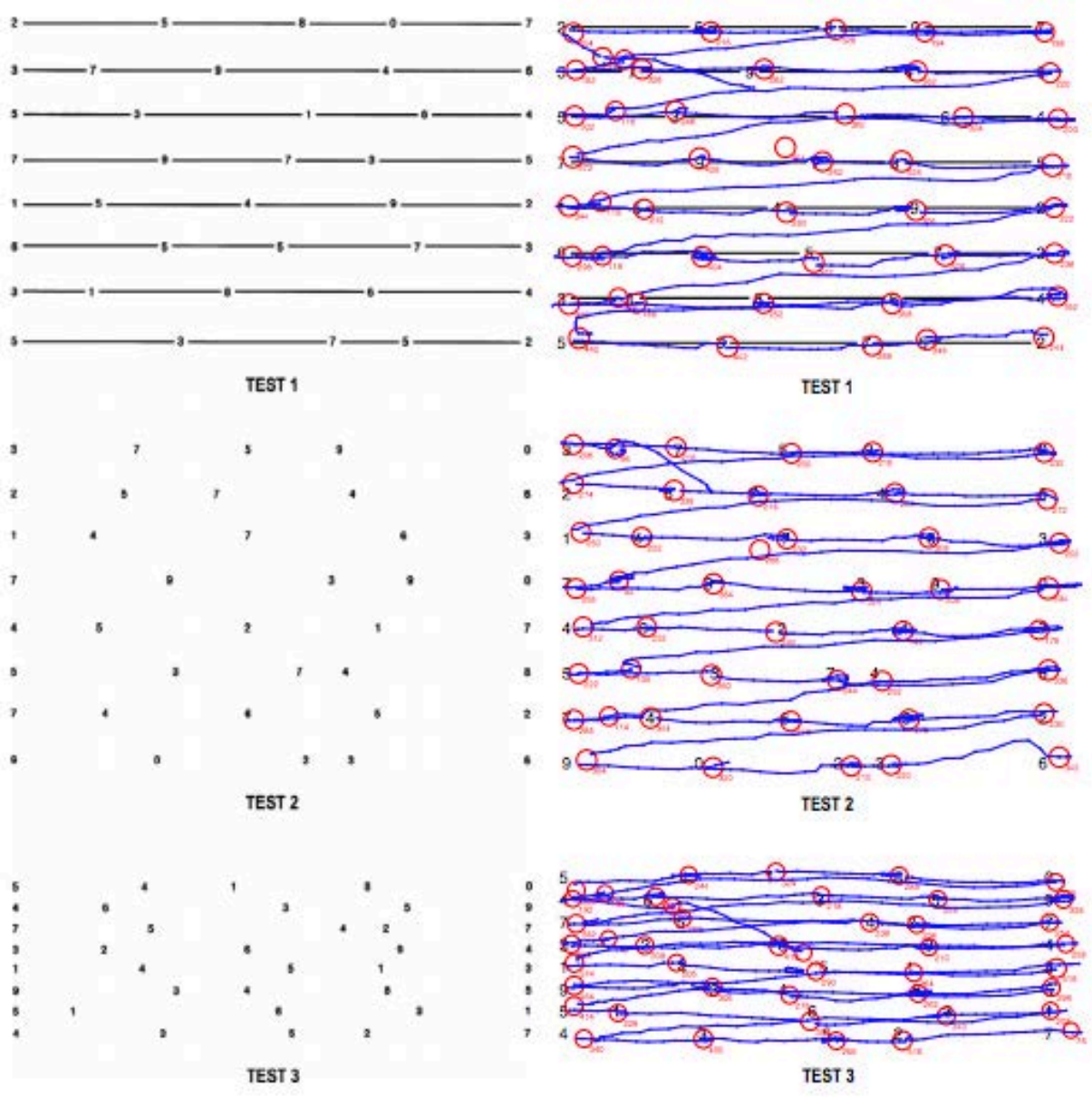

Figure 4. Demonstration of eye tracking during King-Devick Test. *Left cards show the projected King-Devick Test cards in succession Test 1 to Test 3. Cards on the right are illustration of eye tracking from a control subject using infrared oculography. Blue lines illustrate task-specific horizontal and oblique saccades while red circles show where there was a pause for the subject to focus and read the number. Reproduced from Rizzo et al.*[43]

King-Devick Test and Sleep Deprivation

Sleep deprivation, like mild traumatic brain injury, is known to negatively impact ocular-motor and cognitive function and should thus, negatively affect King-Devick test performance. To date, there is merely one study examining King-Devick performance under sleep deprived conditions. Davies et al. found that, while there was improvement between baseline and post-test in both the sleep deprivation group and the control group, the grade of improvement was correlated to the amount of sleep and the sleep deprived group was less improved.[45] These results also support the learning effect seen in non-concussed cohorts. However, the sleep deprived group slept 6 hours or less, which may not be enough to create true sleep deprived conditions.

Conclusion

Due to its high sensitivity, ocular-motor measurements are reliable assessment tools to evaluate brain function. Sleep deprivation, extremely prevalent amongst adolescents and young adults, has many negative adverse side effects to both acute and chronic sleep deprivation, while there are several benefits to prolonged sleep. Saccades, near-point of convergence, and smooth pursuits are prone to deterioration due to sleep deprivation. The King-Devick Test, relying on saccadic eye movement, is a valid and reliable test to detect abnormal brain function as a result of concussion. It remains to be investigated how the King-Devick Test, as dependent on saccades, is affected by sleep deprivation.

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APPENDIX C:

IRB DOCUMENTS and STUDY PROCEDURES FORMS

Acute effects of sleep deprivation and subconcussive impacts on ocular-motor and neurocognitive functions: a pilot study

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1.0 Background

A subconcussive head impact is defined as an impact to the head that does not cause any symptoms of concussion. However, these subconcussive impacts have the potential to cause insidious effects in the brain if sustained repetitively.[1] An average athlete in contact sports (i.e., soccer, football) experiences nearly a thousand subconcussive hits per season,[2] and recent reports from our research team have demonstrated that the repetitive subconcussive head impacts blunts ocular-motor functions.[3,4] Additionally, compelling evidence led us to believe that eye-movement parameters are particularly vulnerable to lack of sleep.[5-8] An increasing number of student-athletes experience sleep deprivation due to academic and sport responsibility (i.e., study hall, exams, team meetings). Consequently, many of student- athletes are exposed to combination of sleep deprivation and subconcussive head impacts. However, it remains unknown whether sleep deprivation combined with subconcussive head impacts may induce additive impairments on ocular-motor functions compared with a single event (sleep deprivation or subconcussive impact only).

Ample research suggests that less than 10% of high school and college students meet the ideal sleep duration of 7-9 hours per night. Limited sleep duration elicits adverse symptoms, which are similar to concussion: headache, fatigue, depressed mood, and difficulty concentrating.[6,9,10] Importantly, recent discovery of the brain lymphatic system, referred as the glymphatic system, underpins the importance of sleep. During sleep state, brain cells reduce their size to allow the movement of interstitial fluids. Debris and toxic factors produced from the cells can be cleared via the glymphatic mechanism.[11,12] Sadly, our society inevitably exposes young adults to competitive challenges (maintaining scholarship, high GPA, superior performance in sports). These duties obligate students to reduce the amount of sleep, while practicing sports more intensely than ever. Therefore, the proposed pilot project is to examine combination effects from partial sleep deprivation coupled with subconcussive head impacts on eye-movement parameters and neurocognitive functions.

Ocular-motor Functions

Ocular-motor function can be measured by quantifying the succession and efficiency of eye movements including saccades, smooth pursuits, and convergence. Saccadic eye movements coupled with smooth pursuits allow individuals to 1) follow moving objects efficiently, 2) accurately predict target trajectory, and 3) change their focus from one object to another smoothly and rapidly.[13] Another ocular-motor function, a near-point of convergence, is the closest point one can visualize an object before diplopia occurs, facilitating people to focus on objects near their eyes, such as reading.[14]

The instruments used to measure ocular-motor function include visual eye tracking devices for saccades and smooth pursuits, the King-Devick test for saccadic velocity and accuracy, and a Breen's Ruler for near point of convergence. These metrics enable researchers to delineate how the brain functions in a healthy state, as well as a pathological state.[15] When the brain is not preforming in an optimal state, abnormalities in ocular-motor function can be observed, such as in a state of sleep deprivation [16,17] and after repetitive subconcussive events or a single concussive event.[18-20]

Subconcussion

Although it largely depends on a type of sports and practice style, average athlete in college football burdens approximately 900 impacts, 16,000 g linear force, and 1,000,000 rad/s^2 rotational force per season.[2] While a concussive impact elicits clinical symptoms (i.e., headache, fatigue, difficulty concentrating, loss of consciousness, and dizziness), subconcussive head hits do not elicit notable concussion-like symptoms regardless of the frequencies and magnitudes of impacts sustained.[3,21] Emerging evidence suggests that subconcussive impacts are dangerous when they are repetitive in nature. Although the causality remains elusive, a number of clinical studies indicate that the accumulation of impacts may lead to chronic neurological deficits.[1,4,22-27] It has also been suggested that an individual who receives repetitive subconcussive head impacts is more susceptible to sustain a concussion.[28-30] Although asymptomatic, studies using sensitive and high- technology measurements began to unravel "subclinical" change in neural function following subconcussive impacts.[31-33] For example, decreased neuronal connectivity was detected via functional magnetic resonance imaging (fMRI) in rugby players who received repetitive subconcussive hits during a game.[34] Furthermore, our soccer heading model applying 10 headers revealed transient defects in the vestibular function.[31] Several studies highlighted the ocular-motor vulnerability in response to traumatic forces to the brain in a severity dependent manner. For example, a notable decline in saccades—rapid changes in eye orientation—has been observed in concussed boxers, football, and rugby players.[35,36] Similarly, a near point of convergence (NPC), which is the closest point one can visualize an object before diplopia occurs, was impaired 3-fold in concussed athletes and soldiers.[20,37] Previously, for the first time we have demonstrated that repetitive subconcussive head impacts could worsen the near point of convergence by 30~40% in soccer 4 and football players.[3] Limited literature available for the effects of subconcussive impacts (Table 1).

Table 1. Research studies examining the effects of subconcussive impacts

Author	Subjects	Method	Outcome
Kawata et al. (2016)	29 college football players	Head impacts monitored via sensor-installed mouth guard	Players with high frequencies of head impacts worsened ocular-motor function, while players with low frequencies remain stable from baseline.
Kawata et al. (2016)	20 college soccer players	10 headings at 25mph	Significant decrease in ocular-motor function immediately after and 24-hours post heading
Gutierrez et al. (2014)	17 high school female soccer athletes	15 directional headers	NSD in neurocognitive function
Munce et al. (2015)	22 youth football players	In-helmet sensors; ocular-motor testing	252 average head impact per season NSD in neurological function

Sleep Deprivation

While optimal sleep may improve mood, function, and performance of student-athletes,[38,39] sleep deprivation is firmly known to trigger negative symptoms such as headache, fatigue, depressed mood, difficulty concentrating, and decreased alertness, reaction times, and cognitive function.[6,9,10] Sleep deprivation is known to impact one's cognitive function, especially requiring memory and speed. For example, a study reported that sleep-deprived college students completed tasks with longer duration and more errors, compared with those who maintain optimal sleep

duration.[40] Further, sleep deprivation has been found to impact the frontal lobe; thus, affecting decision making process in young adults.[41,42]

Eye-movement parameters (saccades, near-point of convergence, and smooth pursuit) are particularly sensitive to quality and quantity of sleep duration, given that neural networks required to control eye movement are highly ubiquitous (Figure 1).

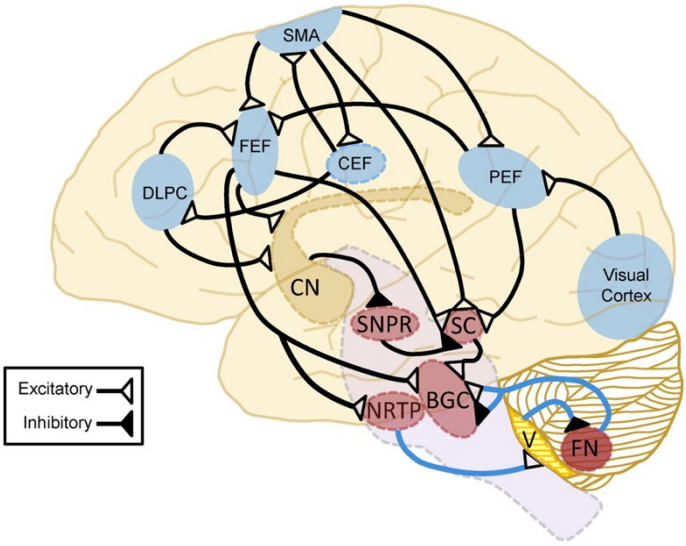

Fig 1. Cortical and subcortical pathways involved in eye movement. In the direct pathway, saccades are initiated when the frontal eye field (FEF) or parietal eye field (PEF) sends signals to the superior colliculus (SC) which then projects to the brainstem gaze centers (BGC). In parallel, the FEF also initiates saccades via direct connections to the BGC. The cingulate eye field (CEF) sends signals to the other eye fields in the frontal lobe. In the indirect pathway, the FEF via the caudate (CN) inhibits the substantia nigra pars reticulata (SNPR), thereby inhibiting the SNPR's inhibition of the SC and allowing saccade generation. Figure reproduced from Ventura et al. (2016).

The EYE-SYNC modality has been used to quantify eye movement demonstrating 88% sensitivity and 87% specificity in detecting mild traumatic brain injury.[28] Continuous gaze- target synchronization during target tracking is dependent on attention, an area affected by sleep deprivation. After 22-hours of sleep deprivation, ocular-motor deficits particularly in smooth pursuit were detected by the EYE-SYNC model.[43] The deficits in smooth pursuit were illustrated by a significantly higher variability in radial and tangential errors after 22 hours without sleeping.[17,43,44]

The linkage between sleep restriction and decreased saccadic velocity was corroborated by several studies.[6,8,45,46] Notably, groups that underwent less than 24-hours of sleep deprivation did not have significant differences in saccadic velocity.[6,7,47] In the studies examining total (24 hours) and extended (more than 24 hours) sleep deprivation, saccadic velocity was decreased acutely after more than 24 hours of sleep deprivation[6,8,45,48,49] but one night of recovery sleep reversed the delayed saccadic velocity. [6,8] Existing research examining the effects of sleep deprivation on ocular-motor function is organized in Table 2.

Table 2. Research studies examining the effects of sleep deprivation on ocular-motor function

Author	Subjects	Hours of Sleep Deprivation	Outcome
Crevitis et al. (2003)	21 medical students	20 hours	No significant difference (NSD) in latency or number of errors
De Gennaro et al. (2000)	9 healthy subjects	40 hours	NSD accuracy of smooth pursuit; Saccadic velocity significantly deteriorated

Fimm et al. (2016)	13 healthy males	24 hours	NSD in saccadic reaction times; Saccadic velocity significantly deteriorated
Fransson et al. (2008)	10 healthy males 8 healthy females	24 hours 36 hours	NSD in smooth pursuit accuracy between 24- and 36-hour wakefulness groups; NSD in saccadic accuracy; Decreased performance of saccadic velocity
Zils et al. (2005)	15 healthy males	24 hours	Peak saccadic velocity increased; NSD between baseline and testing after 1 night of recovery sleep
Rowland et al. (2005)	12 healthy subjects	20 hours followed by 64 hours	Significant increase in saccadic velocity after 64-hour NSD in saccadic velocity in 20-hour group; NSD between baseline and post-sleep deprivation measures after 1 night of recovery sleep
Goldrich et al. (2010)	5 male; 8 female	24 hours 26 hours 28 hours	NSD in saccadic velocity after 24- and 26- hours of wakefulness Significant decrease in saccadic velocity in 28 hour
Russo et al. (2003)	57 commercial drivers	7 consecutive nights of: 21 hours 19 hours 17 hours 14 hours	NSD 14-hour and 17-hour groups Saccadic velocity significantly increased in 19-hour and 21-hour groups

Ocular-Motor Modalities

King-Devick Test

The King-Devick Test (Figure 2) has been found to be a reliable test used to detect the presence of a concussion or mild traumatic brain injury.[28,50-52] The test takes approximately two minutes to complete. After completing a demonstration card, the subject orates the numbers spread out on three cards as fast and accurately as possible; both time and number of errors are recorded. With the saccadic eye movements combined with the cognitive function of reading numbers, the King-Devick test examines the function of multiple facets of the brain including eye fields (frontal eye fields, supplementary eye fields), dorsolateral prefrontal cortex, cerebellum, cerebral cortex, and deeper structures of the brain stem.[15,51,52] It is noteworthy that the King-Devick Test isolates and examines saccadic function..[20] An increased time to complete the test in relation to baseline indicates the presence of neural delay.

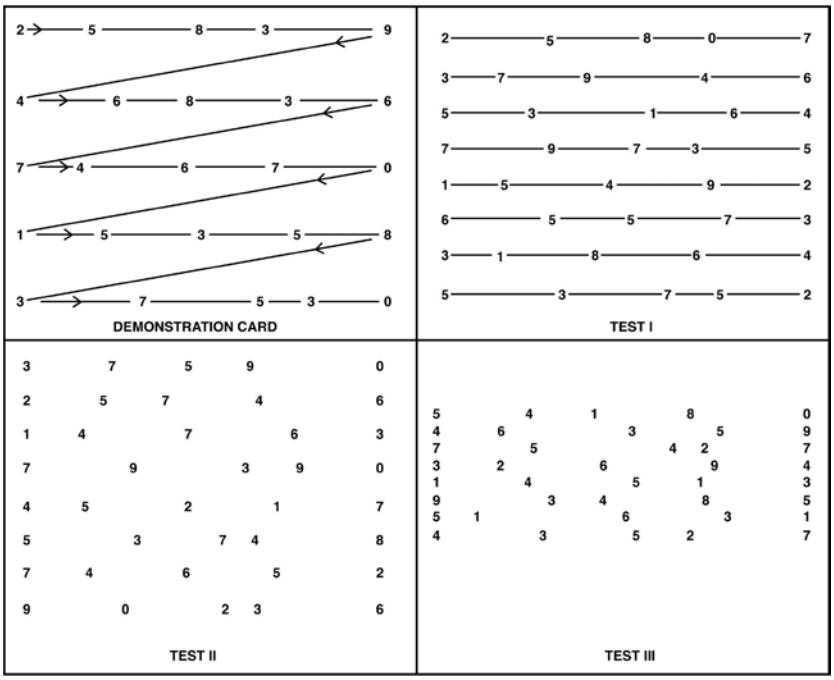

Figure 2. King-Devick Test Cards. King-Devick Test, which consists of 1 demonstration card and 3 test cards. Participants are instructed to read the numbers on each card from left to right as quickly as possible without making any errors. The sum of the time scores from all 3 test cards is the summary score or K-D time score for the entire test. The number of errors made in reading the test cards is also recorded. *Reproduced from Leong et al.*

EYE-SYNC Ocular-Motor Headset

When a moving target is visually tracked, there is a time lag between visual information from the eyes to the brain and motor signals from the brain to the eye muscles. The brain circumvents the neural delay by using spatial and temporal predictions, thus one can track the moving object smoothly.[53] This dynamic gaze-target synchronization is achieved by smooth pursuit of eye movement and prediction. At each time point we will employ a circular visual-tracking paradigm using the ocular-motor headset (Figure 3: EYE-SYNC, SyncThink, Boston, MA), with the target traveling at a constant angular velocity with a fixed radius from the center (Figure 4).[54] Previously, this metric yielded 88% sensitivity and 87% specificity in detecting concussion.[55] Our test-retest internal validation with 1 week apart in 10 healthy college-aged adults resulted in $r = 0.92$ for variabilities of the smooth pursuit velocity gain and $r = 0.89$ for gaze position error variabilities. During preparation, subjects will be seated in a dimmed room and wear the headset. Subjects' eye position as well as gaze capture quality will be calibrated using 9-point calibration maneuver where both eyes follow a target presented in 9 spots in the visual field sporadically. For the testing, the subjects will be instructed to track a visual stimulus (small red circle) moving in a clockwise circular trajectory of 10° radius at 0.4 Hz for 36 seconds in the headset monitor. Movements of both eyes will be recorded. To obtain the smooth pursuit velocity gain, sine curves with the circular movement of the target will be fit to the horizontal and vertical eye velocities using

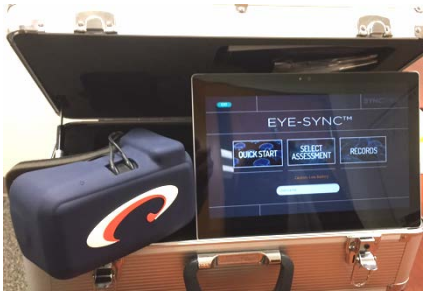

Figure 3. EYE-SYNC ocular-motor headset. A screen inside the headset (left) projects a circular target and one must follow the target as close as he/she can. Data captured by an installed camera within the headset will be transferred to the Windows tablet (right).

fast Fourier transformation. The ratios between the eye and target velocities in the horizontal and vertical directions will be computed. Gaze position error variability is characterized by the standard deviation of gaze positional errors relative to the target.[56]

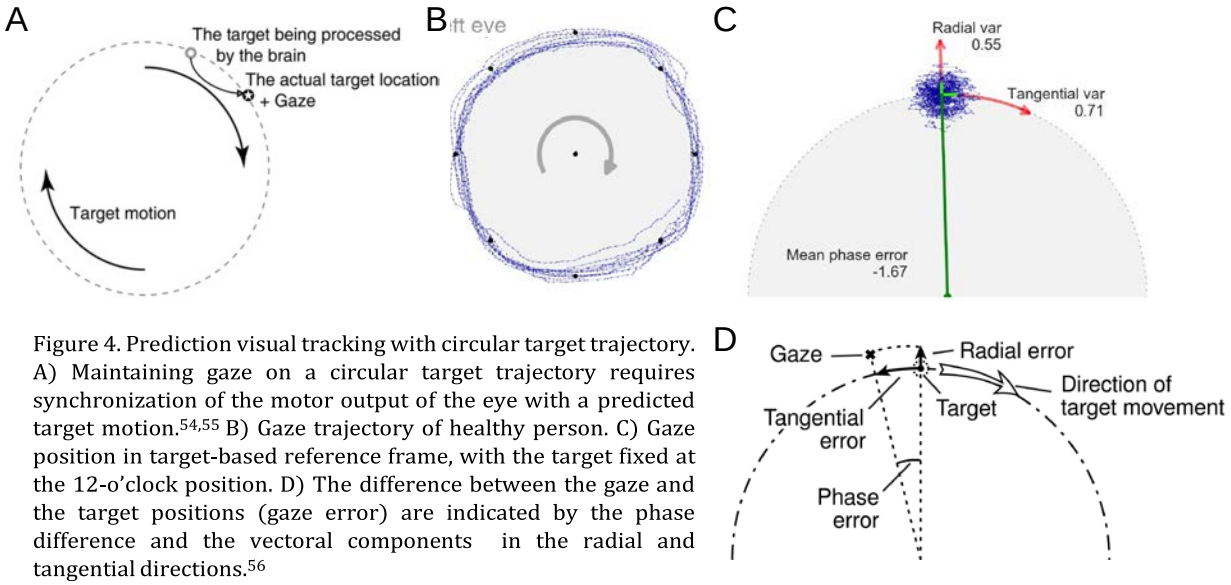

Figure 4. Prediction visual tracking with circular target trajectory. A) Maintaining gaze on a circular target trajectory requires synchronization of the motor output of the eye with a predicted target motion.[54,55] B) Gaze trajectory of healthy person. C) Gaze position in target-based reference frame, with the target fixed at the 12-o'clock position. D) The difference between the gaze and the target positions (gaze error) are indicated by the phase difference and the vectoral components in the radial and tangential directions.[56]

Neurocognitive Function

Although immediate declines in verbal and visual memory, and complex reaction speed have been noted after a concussion,[57] reports on the subconcussive effect remain scarce. However, it is firmly established that the years of cumulative exposure to subconcussive head impacts manifests changes in mood, neurocognitive function, and brain structure.[1,58,59] A definitive causality between head hits and early onset of CTE is yet to be determined, but it is suggested that repetitive subconcussive head impacts portends depressive characteristics in former football players, as nearly 40% of retired NFL players had mild to moderate symptoms of depression.[60,61] A recent study further indicates that season-long heading exposures in amateur soccer players (Avg. 432 headers) were linked to lower integrity in neuronal axon in the tempo-occipital white matter, measured via the diffusion tensor magnetic resonance imaging (MRI). Strikingly, these results are coupled with poorer performance in the memory test compared to the pre-season baseline.[62] The neurocognitive functions after acute soccer headings, using the exact protocol as our study, has never been tested. However, acute bouts of soccer heading appears to have a minimum influence on neurocognitive functions.[63] Similarly, chronic sleep deprivation is known to blunt neurocognitive function, further leading to early onset of dementia.[64] Although a single bout of acute sleep deprivation shows unobservable effects on neurocognitive performance,[65,66] the effects become prominent as sleep quality and quantity decreases repeatedly.[67] There is, however, a fundamental knowledge gap in the effects of reduced sleep duration coupled with subconcussive head impacts on neurocognitive function.

Soccer Heading Modality

Soccer heading is a common skill performed by soccer athletes during practice and games. An average collegiate soccer players perform about 500 headers during a single season and over 3000 during the course of a career [68,69] Research has demonstrated the need for increased awareness of potential brain injury associated with heading the soccer ball as some researchers suggest that the cumulative effect of soccer head impacts over a career may lead to outcomes similar to sustaining multiple concussions.[70] Various studies have been conducted to examine the effect of an acute bout of soccer heading, including Dr. Kawata's previous laboratory at Temple University, with most authors reporting no significant effect of heading on the brain function measures of neuropsychological or balance performance. We have tested collegiate soccer players post heading ball speed up to 50 mph with no significant alterations in common clinical measures (e.g., balance error scoring system, signs and symptoms checklist). However, sensitive modalities like blood biomarker and ocular-motor testing begin to unravel subclinical perturbation caused by minor head hits if sustained repetitively.[3,4,31] Table 3 highlights existing research studies examining the effects of an acute bout of soccer heading.

Table 3. Research studies examining the effect of an acute bout of soccer heading

Author	Subject	Method	Outc
Patuklan et al. (2000)	100 college athletes	20 minutes of practice heading	NSD in neuropsychological performance
Brogilo et al. (2004)	40 college athletes	20 headers in 20 min.	NSD in postural control
Magnus et al. (2004)	10 college athletes	20 headers in 5 min.	NSD in balance
Schmitt et al. (2004)	31 college athletes	18 headers in 40 min.	NSD in postural control Symptoms increased (headache, vertigo, fatigue)
Mussack et al. (2003)	Amateur athletes 61 heading group 58 active controls	55 min of heading practice Exercise	Significant increase in astrocyte-enriched blood biomarker (S-100B) in heading versus active control
Staiancke et al. (2004)	44 professional athletes	Soccer game	Significant increase in S-100B, + correlation between S-100B and # of headers
Otto et al. (2005)	Adult athletes	Boxing Marathon Running Soccer Heading (16mph)	Significant increase in S-100B Significant increase in S-100B NSD in S-100 B
Haran et al. (2013)	16 college athletes	Soccer heading (25 mph)	Significant change in postural control using virtual environment 24h post.
Zetterberg et al. (2007)	23 amateur soccer players 10 non-athletic subjects	20 headings	NSD in 100B between pre vs. post and heading vs. control group
Dorminy et al. (2015)	16 college soccer players	5 headings at 30, 40, 50 mph	NSD in S100B nor concussion symptoms after soccer heading at any speed
Kawata et al. (2016)	20 college soccer players	10 headings at 25mph	Significant decrease in ocular-motor function immediately after and 24-hours post heading
Hwang et al. (2016)	20 college soccer players	10 headings at 24mph	Significant change in vestibular function immediately after headings but NSD in 24h post-heading
Kaminski et al. (2007)	71 college soccer players	Pre-post season	NSD in balance, neurocognitive performance

Kontos et al. (2011)	63 youth soccer players	Heading exposure groups High vs. Moderate vs. Low	NSD in neurocognitive performance between groups
Gutierrez et al. (2014)	17 high school female soccer athletes	15 directional headers	NSD in neurocognitive function

2.0 Rationale and Specific Aims

Because our primary aim of the proposed pilot study is to estimate the combined effects of sleep deprivation and subconcussive head impacts on ocular-motor and neurocognitive functions, the goal has been set to observe the potential trends in outcome parameters after combined interventions.

Aim 1-1: To examine the acute effect of sleep deprivation on saccadic velocity, near- point of convergence, and smooth pursuit

Hypothesis 1-1: There will be significant declines in saccadic velocity, near-point of convergence, and smooth pursuit after partial sleep deprivation.

Rationale: Ample research suggests that less than 10% of high school and college students meet the ideal sleep duration of seven to nine hours per night.[6,9,10] Ocular- motor functions are known to negatively correlate with sleep depravity. For example, the peak velocity of saccadic movements was significantly reduced after one night of total sleep deprivation.[8] After the acute sleep deprivation, researchers found that eye-movement parameters were normalized to baseline following one night of recovery sleep.[6,8] Similar to the acute state of total sleep deprivation, partial sleep deprivation has been shown to impair ocular-motor function.

Aim 1-2: To examine the acute effects of subconcussive impacts on saccadic velocity, near-point of convergence, and smooth pursuit.

Hypothesis 1-2: There will be significant declines in saccadic velocity, near-point of convergence, and smooth pursuit after subconcussive impacts.

Rationale: Concern emerges when examining the effects of subconcussive impacts on ocular-motor function. To date, a paucity of research has examined the effects of subconcussive impacts on the ocular-motor system. This raises alarm as high school and college athletes suffer anywhere from a couple hundred to a thousand head impacts per season.[2,71] Concussion is known to perturb an entire ocular-motor function,[20,36,72] and recent preliminary works have shown a similar trend with less magnitude of impairment particularly in near point of convergence.[3,4]

Aim 2: To estimate the combined effects of sleep deprivation and subconcussive head impacts on saccadic velocity, near-point of convergence, and smooth pursuit.

Hypothesis 2: There will be significant declines in saccadic velocity, near-point of convergence, and smooth pursuit in the combined sleep deprivation and subconcussive impacts group compared to the individual sleep deprivation or subconcussive impacts groups.

Rationale: The deterioration of ocular-motor function, as seen individually caused by sleep deprivation or subconcussive impacts, reflects brain function and may impact the success of performances. When this information is applied to the reality of school sports and the sleep-deprived athletes, it is worrying. The negative effects of sleep- deprivation and subconcussive impacts on ocular-motor function and the reality and prevalence of both sleep deprivation and subconcussive impacts warrants investigation.

Aim 3: To estimate the combined effects of sleep deprivation and subconcussive head impacts on neurocognitive function.

Hypothesis 3: There will be significant impairments in neurocognitive parameters in the combined sleep deprivation and subconcussive impacts group compared to the individual sleep deprivation or subconcussive impacts groups.

Rationale: Our previous study has shown that subconcussive head impacts do not alter neurocognitive functions (i.e., complex reaction speed, verbal and working memory). However, when one is subjected to partial sleep deprivation followed by subconcussive head impacts, likely that one's neurocognitive processing speed will be perturbed.

3.0 Inclusion/Exclusion Criteria

Inclusionary criteria will include:

1. being between 18 to 26 years of age
2. an active member of a soccer team (i.e., collegiate, intramural, club, professional)
3. at least 5 years of soccer heading experience
4. normal or corrected-to-normal vision
5. regularly sleeps between 7h00min and 9h00min per night, validated by subjective sleep log and ActiGraph monitor

Exclusionary criteria will include:

1. any head, neck, or face injury in the six months prior to the study (e.g., concussion, eye injury);
2. history of vestibular, ocular, or vision dysfunctions (e.g., macular degeneration);
3. pregnancy;
4. any neurological disorders (e.g., seizure disorders, closed head injuries with loss of consciousness greater than 15 minutes, CNS neoplasm, spinal cord injury/surgery, history of stroke)
5. any sleep disorders (e.g., sleep apnea, insomnia)
6. lower extremity injury that would prohibit normal walking
7. metal implants in the head
8. prescription of caffeine
9. implantation of cochlear device, cardiac pacemaker, medical fusion device, intracardiac lines, or neurostimulator (e.g., DBS, epidural/subdural VNS);
10. history of severe injury to the bones, joints, or muscles in either arm;
11. glasses are prohibited (contact lens are okay) for safety purpose for the heading intervention
12. using sleeping pills (i.e., melatonin)

Session-specific exclusion criteria will include:

1. drank more than 1 alcoholic drinks or used recreational drugs 24 hours before the 1st and 2nd day test day
2. consumed caffeine while enrolled in the study
3. slept for any duration of time when explicitly instructed not to do so

4.0 Enrollment/Randomization

Potential participants will be recruited via listserv email to undergraduate and graduate students in the School of Public Health-Bloomington, as well as flyers posted in the School of Public Health Building. Interested participants will contact (phone or email) and meet with the investigator to discuss the project and ask questions. The informed consent and Concussion History & Health History Questionnaire will be given to the potential candidates. Also, the sleep log sheet and wrist-band based activity/sleep monitor (ActiGraph) will be provided to the potential participants to record sleep duration (not a rest duration) for a week prior to the study. The ActiGraph reads one's sleeping duration and depth of sleep, which has been known to be useful in distinguishing sleep from resting. If the participants meet the inclusion criteria and are free of exclusionary factors will advance to the testing procedures.

Based on the order of subject participation, Dr. Kawata will assign subject number: i.e., subject 1 is the 1st person in the study. Dr. Zhongxue Chen will generate randomly stratified codings (1 – 40) that correspond to study group. For instance, subject numbers 2, 5, 10, 11, 18, 22, 24, 29, 33, 34 will be assigned to Group 1, and subject numbers 1, 6, 7, 9, 19, 20, 21, 32, 35, 38 will be assigned to Group 2, and so on for Groups 3 and 4. As a result, we will still ensure an unbiased group assignment.

Sleep deprivation and soccer heading interventions will be conducted by Dr. Kawata and his research assistants, Mr. Krueger and Ferris. Ocular-motor testing and neurocognitive functions will be performed by Ms. Coon, who is a certified ImPACT tester and well trained to measure ocular-motor parameters. Ms. Coon will be blinded for subjects' group assignment. Statistical analyses of all the data will be performed by Dr. Chen.

Group Characteristics

Control Group

Subjects in the Control group will not be subjected to sleep deprivation nor subconcussive head impacts; hence, the subjects will sleep regularly at home and perform soccer kicking (instead of soccer heading). This way, we will ensure these subjects are free of sleep deprivation and subconcussive effects.

Subconcussion Group

Subjects in the subconcussion group will not be subjected to sleep deprivation and will sleep regularly between tests 2 and 3 at home. The subjects will undergo the soccer heading intervention between Test 3 and Test 4. This allows us to isolate the effects of head impacts on the ocular-motor and neurocognitive function.

Partial Sleep Deprivation Group
Subjects in the sleep deprivation group will be allowed to sleep from 3:00 to 7:00 in the lab between Day 1 and Day 2 to safely induce partial sleep deprived conditions. The subjects will perform soccer kicking (instead of soccer heading) during the intervention between Test 3 and Test 4. This ensures isolation of the effect(s) of sleep deprivation on ocular-motor and neurocognitive function.

Combination Group (partial sleep deprivation with subconcussive head impact)
The combination group will be subjected to both sleep deprivation and soccer heading. The subjects will be allowed to sleep from 3:00 to 7:00 on Day 2 to create sleep deprived conditions. Between Test 3 and Test 4, the subjects will undergo the soccer heading intervention. This way, we can discover the combined effects of sleep deprivation and soccer heading on ocular-motor and neurocognitive function.

5.0 Study Procedures

Research Design
We will use a 4 x 4 repeated measures design. The independent variables will be Time [baseline (Test 1), pre-sleep (Test 2), post-sleep/pre-heading (Test 3), and post-heading (Test 4)] and Group (control, partial sleep deprivation, subconcussion, and partial sleep deprivation combined with subconcussion) as depicted in the study design below (Figure 5). Our primary interest is to observe changes in the ocular-motor and neurocognitive functions following partial sleep deprivation coupled with subconcussive head impacts from soccer headings.

Figure 5. Study design.

	Day 1				Day 2		
GROUP / TIME	0800		2000		0800		0815
	Test 1 (Baseline)	Day	Test 2	Sleep Schedule	Test 3	Intervention	Test 4
Control		No sleep		Normal		Kicking	
SD		No sleep		0300-0700		Kicking	
Sub-C		No sleep		Normal		Heading	
SD + Sub-C		No sleep		0300-0700		Heading	

NOTE: Sleep Deprivation (SD); Subconcussion (Sub-C)

The study consists of 4 data collection time points in a 2-day period. Test 1 will be the baseline and measured at 8am on the 1st day. Test 2 will be measured at 8pm on the 1st day to evaluate the potential fluctuations in outcome parameters between the morning and night time. Test 3 will be measured at 8 am on the 2nd day, which will evaluate the effects of sleep deprivation within- and between-groups. Simultaneously, Test 3 will serve as a pre- subconcussion time point. Test 4 will be conducted after soccer heading or kicking intervention. This longitudinal study design with appropriate grouping variables enables us to interpret effects from sleep, head impacts, and the combination of both.

The testing duration is estimated to be 30 minutes for each of the four data collection time points. After Test 2 at 8pm, for sleep deprivation groups (SD+kicking and SD+Subconcussion), the

subjects will stay in the sleep lab in the School of Public Health until next morning with a total of 12h commitment (8pm till 8am). Subconcussion intervention will last 10 minutes. Breakdowns of subject time commitment per group are followings:

Group	Total	Test 1	Test 2	Sleep Intervention	Test 3	Soccer Intervention	Test 4
Control	2h 10min	30min	30min	n/a	30min	10min	30min
Sub-C	2h 10min	30min	30min	n/a	30min	10min	30min
SD	14h 10min	30min	30min	12h	30min	10min	30min
SD + Sub-C	14h 10min	30min	30min	12h	30min	10min	30min
NOTE: Sleep Deprivation (SD); Subconcussion (Sub-C)							

For this pilot study, we propose to include 10 subjects per group (total 40 subjects). We estimate data collection and primary analysis of 40 subjects will last approximately 15 months.

Partial Sleep Deprivation Protocol

A week prior to the study, the ActiGraph wGT3X-BT will be given to subjects, which will monitor activity and sleep cycles. Additionally, the subjects will be instructed to record their sleep log (attached file). Subjects who sleep a minimum 7 hours per day will proceed to the study. Subjects in all groups will continue to wear the ActiGraph wGT3X-BT until the end of the study duration. We will use a modified version of partial deprivation protocol[7,47], which will restrict sleep duration within 4 hours for the sleep deprivation groups. Following the Test 2 time-point, subjects in the sleep deprivation and sleep deprivation with subconcussion groups remain in the sleep lab from 20:00 on Day 1. The subjects are instructed to bring comfortable clothes. Between 20:00 and 3:00, subjects are allowed to engage in sedentary activities, including reading, studying, playing video games, watching movies, and light walking in the sleep lab. Subjects are allowed to drink water *ad libitum*. A snack (chocolate bun) will be provided at 22:00. An experimenter will stay in the sleep lab between 20:00 and 3:00 to ensure whether subjects are complying with the rules or not. At 3:00, an experimenter will prepare sheets and blankets for each subject, instruct subjects to sleep until 7:00, turn off the lights, and exit the lab. For this pilot study, we will employ the ActiGraph wGT3X-BT to monitor participants sleeping pattern (wake/sleep duration), rather than using an electroencephalography during the sleep. At 7:00, an experimenter will wake the subjects up and a standard warm breakfast (bagels with butter or cream cheese) will be provided. Subjects are allowed to take a shower; however, caffeinated drinks (i.e., tea, coffee, soda) are prohibited. Instead, decaffeinated drinks are allowed.

Sleep Lab

The sleep lab located in the Indiana University School of Public Health, C214, is equipped with necessary modalities and amenities to conduct sleep studies. The lab has a carpeted floor with 9

clinical twin-sized beds, electroencephalography (EEG), and oxygen supply. The present pilot study does not measure the sleep quality via brain wave monitor using EEG and breathing pattern using oxygen monitor, rather we will utilize the ActiGraph wGT3X-BT to monitor the duration of night sleep, as described in the protocol above. The bathroom is located 10 steps away from the lab and shower facility is located in the basement of the facility.

Soccer Heading Protocol

Based on the simple randomization described in the Enrollment and Randomization section, subjects will be randomly assigned into one of two groups for the intervention (heading or kicking-control). The heading intervention intends to account for the effect of mild head impacts, while the kicking group will serve as a control group given activity levels between groups are similar with the only difference in head impacts. A standardized and reliable soccer heading protocol will be used for the experiment. A triaxial accelerometer (Triax Technologies) embedded in a head-band pocket and positioned directly below the external occipital protuberance (inion) will monitor linear and rotational head accelerations. A JUGS soccer machine will be used to simulate a soccer throw-in. A standardized ball speed of 25mph will be used across both heading and kicking interventions. The ball speed is similar to when soccer players make a long throw-in from the sideline to mid-field. Soccer players frequently perform this maneuver during practices and games. Subjects will stand approximately 40 feet away from the machine to perform either the heading or kicking (Figure 6). Dr. Kawata's previous laboratory at Temple University has routinely employed the protocol; the average linear head acceleration yielded from the header is 14.5g. Many subconcussion studies in football and ice hockey set a threshold of impact recording as 16g, indicating

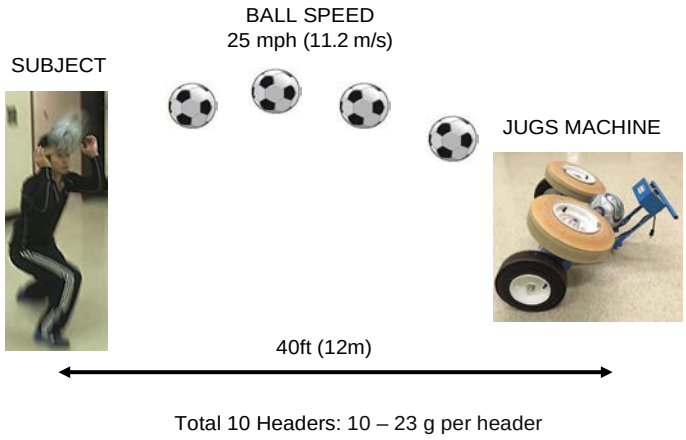

Figure 6. Mild head impact intervention, previously used in our previous works (Kawata et al. 2016; Hwang et al. 2017)

that impacts induced from our protocol are below the minimum magnitude recorded in other contact sports. Participants in the subconcussion group and sleep deprivation with the subconcussion group will perform 10 standing headers with 1 header per minute, whereas participants in the control group and sleep deprivation group performs 10 kicks at a cadence of 1 kick per minute. The subjects will be instructed to direct the ball back toward the JUGS soccer machine in the air, for both heading and kicking.

Ocular-Motor Assessments The EYE-SYNC Headset

The subject will perform eye-movement tasks using the EYE-SYNC headset. This visual- tracking protocol has been replicated and validated in numbers of concussion and sleep deprivation studies,[16,17,53,54,73,74] however to our knowledge this study for the first time will unravel subconcussive effects. Prior to testing, a Snellen chart will be used to verify that the subject has a normal or corrected-to-normal vision (minimum 20/30). The subject will be seated in a normally lit room and stabilize the headset with two hands while the elbows rest on the desk. The visual stimulus will be presented using a 120-Hz frame rate LCD screen in the headset and binocular eye movements will be tracked by a single camera secured in the headset. The test stimulus consists of a red circular target, 0.5° diameter in a visual angle with a 0.2° black dot in the center. The target moves in a circular clockwise trajectory of 10° radius at 0.4 Hz, with the target speed corresponding to 25°/s. The entire testing sequence, lasting approximately 3 minutes, will consist of a calibration and 2 consecutive test runs. Calibration of the eye position is conducted by having the subject fixate on a target presented at eight locations on the circular path of the test stimulus and one additional fixation point at the center of the circular path. The fixation target was presented at these nine locations in a randomized order. Each of the two test runs consists of 6 cycles of circular movement corresponding to 15 seconds in duration per test run. The subject will be instructed to "follow the movement of the target as closely as possible."

Near Point of Convergence

An accommodative ruler (Figure 7; Bernell Incorp. Mishawaka, IN) will be used to assess the near point of convergence (NPC). The NPC measures the closest point to which one can maintain convergence while focusing on an object before diplopia occurs.[13] The participant will be seated with the head in anatomical position. Participants will wear contact lenses if needed. The accommodative ruler will be placed to rest on the participant's upper lip, and an accommodative target (reduced-size Snellen chart) will be adjusted horizontally to participant's eye level. The participants will be instructed to maintain gaze on a 14-point font size letter "T". The target will be moved down the length of the ruler, towards his/her eyes, at a rate of approximately 1 to 2 cm/s. The near point of convergence measurement will be taken when eye mal-alignment is observed by the tester or when the

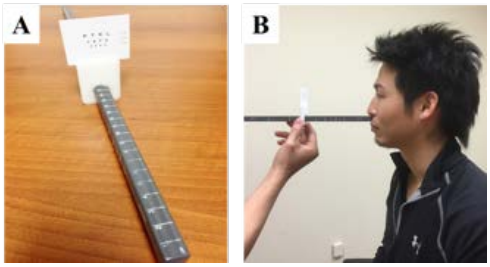

Figure 7. Near Point of Convergence. A) Accommodative ruler. B) When one cannot visualize a letter "T", distance from the bridge of nose is measured. Figures reproduced from Kawata et al.[13]

participant verbally signaled once he/she experiences diplopia and no longer perceives a single target. Upon the verbal signal, the examiner stops moving the target and records the distance between the participant and object. [75] Assessment will be repeated twice and mean NPC scores will be used for statistical analyses. The test takes approximately one minute to complete. The inter-rater reliability of this test was assessed through a pilot study in our laboratory where two testers performed convergence assessments in 8 young, healthy, active subjects, and resulted in a strong association between two testers (Pearson $r = 0.90$, $P < 0.01$).

King-Devick Test

The King-Devick Test is comprised of one demonstration card and three tests cards. The demonstration card is used as a model to familiarize the participant with the test. The test will take place when the participant is comfortably seated and in a well-lit room. The participant will be instructed to call out the numbers on the card from left to right, top to bottom. The participant may not use his/her finger as a reading guide. The number of errors and the time it takes for the participant to complete each card will be recorded on the data collection sheet. The demonstration card is the easiest as it has arrows guiding the participant's vision from one number to the next. Cards one, two, and three increase in difficulty because the guiding lines disappear and the group of numbers becomes denser. The total duration of the test is less than five minutes. By comparing baseline and later performances, changes in saccadic velocity may be identified.

Neurocognitive Assessments

The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) will be used to assess the effects of sleep deprivation and subconcussive head impacts on the neurocognitive function. The ImPACT has been incorporated in athletes, military servicemen, and civilian, yielding one of the highest validities among other computer-based testing [i.e., Automated Neuropsychological Assessment Metrics (ANAM) and Axon Sports].[76] Although the computer-based testing does incur inevitable subjective factors (subjects' mood, fatigue, and time of day), the ImPACT battery shows acceptable test-retest reliability.[77] This particular tool helps to identify compromised neurocognitive functioning in different areas, including attention span, reaction time, problem solving, and working and verbal memory. By comparing subjects' post-intervention scores to their baseline performance, declines in functioning can be identified. The ImPACT takes about 20 minutes to complete. Subjects will be seated in front of a 20-inch desktop, where stimuli are presented on the screen. Subjects will be instructed to "read the instruction and complete the tasks as quickly as you can". Data will be stored in the secured system and extracted for analysis.

Procedure Outline

1. Email distribution.
2. Interested participants contact PI (KK) to discuss Project.
3. Participants meet with the PI to discuss a project and ask further questions.
4. Participants take informed consent form with them and return with signature if they are willing to participate in the study.
5. Participants begin recording sleep log.
6. PI (KK) randomly assigns categories.
7. Participants take sleep log and complete it for one week prior to testing.
8. Test 1
    a. Ocular-motor function (Lab; 10 minutes; SC)
        i. King-Devick Test
        ii. Eye-Sync
        iii. Near-Point of Convergence

    b. Neurocognitive function (Lab; 20 minutes; SC)
        i. ImPACT Test
9. Participants are instructed to remain awake, not to consume caffeine (i.e. coffee, soda, tea), and to return in 12 hours.
10. Test 2
    a. Ocular-motor function (Lab; 10 minutes; SC)
        i. King-Devick Test
        ii. Eye-Sync
        iii. Near-Point of Convergence

    b. Neurocognitive function (Lab; 20 minutes; SC)
        i. ImPACT Test
11. Sleep Deprivation

    Participants in sleep deprived group and sleep deprived with soccer heading group will stay to sleep in the lab (Sleep Lab; 12 hours; KK, RK, MF) Participants in the control group and soccer heading group instructed to return home to sleep normally and to return to the lab in 12 hours.
12. Test 3
    a. Ocular-motor function (Lab; 10 minutes; SC)
        i. King-Devick Test
        ii. Eye-Sync
        iii. Near-Point of Convergence

    b. Neurocognitive function (Lab; 20 minutes; SC)
        i. ImPACT Test
13. **Soccer heading/kicking intervention** (Lab; 10 minutes; KK, RK, MF) Participants in the soccer heading group and sleep deprivation with soccer heading group will complete the soccer heading

    Participants in the control group and sleep deprivation group will complete soccer kicking.
14. Test 4
    a. Ocular-motor function (Lab; 10 minutes; SC)
        i. King-Devick Test
        ii. Eye-Sync
        iii. Near-Point of Convergence

    b. Neurocognitive function (Lab; 20 minutes; SC)
        i. ImPACT Test

6.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

Reporting Adverse Events

Keisuke Kawata, Ph.D. (primary investigator) will serve as the data safety monitor. The data safety monitor will monitor adverse event(s) data, oversee procedures designed to protect the privacy of subjects, and coordinate the reporting of the outcome of any investigation of an adverse event. In the case of an adverse event, Dr. Kawata will report and cooperate with the IRB in any necessary investigation.

Adverse Events Associated with Soccer Heading

There is a risk of inducing symptoms such as headache, blurred vision, and disorientation during soccer heading testing, however ten soccer headers with mild head acceleration are commonly incorporated in soccer practice, and certainly soccer players utilize heading skill to direct a soccer ball for passing and scoring during practice and game. An average soccer player performs 500 headers over an entire season.[68,69] It is extremely unlikely to elicit concussion-like symptoms (headache, nausea, disorientation, blurred vision) from headings with mild head acceleration (Avg. 14.5g). The study protocol has been replicated in multiple laboratories, producing invaluable data to progress traumatic brain injury research. Moreover, our preliminary study in football players have shown that a player sustained 39 head hits with the total magnitude of 1,200g during a single practice, but with no change in symptoms.[3] In order to minimize the risk of adverse events from soccer heading, we will only include soccer players who regularly play soccer and perform soccer headings.

Adverse Events Associated with Partial Sleep Deprivation

There is a risk inducing symptoms such as drowsiness, headache, confusion, blurred vision, fatigue, disorientation, and difficulty in concentration. However, sleep deprivation study has been conducted in various labs, with more than 3000 literature has been published to date. The current study follows partial sleep deprivation protocol restricting sleep duration to 4 hours, which is replicated in a number of studies. Thus, the risk of inducing adverse symptoms is estimated to be minimum. In order to minimize the risk of adverse events from partial sleep deprivation, we will verbally make sure if participants are comfortable proceeding the study.

Adverse Events Associated with Partial Sleep Deprivation Followed by Soccer Heading

The proposed study is the first laboratory study investigating clinical void in the current scientific knowledge. There are numerous clinical investigations test either sleep deprivation or subconcussive head impact effects, however because of lack of knowledge in combined effects, data interpretation remains speculative at best. As described above, our soccer heading and partial sleep deprivation protocols are mild in nature that we (based on our previous data and literatures) foresee no harm nor adverse symptoms from both protocols. However, when both effects are combined, there will be minimum to moderate risks that participants may exhibit slight change in ocular-motor performance and/or neurocognitive function. These data are extremely valuable to ensure the safety of millions of adolescents and young-adults who engage in school duties as well as athletic responsibilities. Each header, we will verbally make sure how participants are feeling. Participants will be instructed to be completely honest of their symptoms, thus we will be able to protect their safety while collecting data that can impact public health guideline in near future.

Adverse Events Associated with Ocular-motor testing

While performing ocular-motor tasks, participants may experience a transient headache and dizziness. Because the ocular-motor testing runs for 15 seconds and is repeated twice, we believe that it is rare to elicit symptoms in the short period of testing. Based on the large- scale normative data (n=50,000) acquired by SynkThink Inc. among sports athletes and military servicemen, no one has claimed abnormal symptom due to the ocular-motor testing. For the near-point of convergence and King-Devick Test, no report has been noted the adverse events associated with the testing, given that the test procedures are self-regulated, meaning subjects control their speed of task performance. Subjects are instructed to terminate or pause their performance if any sign of adverse symptom arises.

Adverse Events Associated with computer-based neurocognitive assessment
The ImPACT neurocognitive assessments impose no medical, legal, or financial risks for participants.

7.0 Study Withdrawal/Discontinuation

Data collection will require subjects to participate in 4 test sessions. Subjects may withdraw from the study at any time. A subject may also be withdrawn from the research without his/her consent if, for example, he/she 1) comes to any test sessions with intoxication, 2) sustained injury prior to any test sessions, 3) self-reported sleep deprivation for the 1st and/or 2nd day, 4) sustained a head injury prior to any test sessions. If the subject completed, for example, entire 1st day procedure (3 test sessions) and unable to participate in the 2nd day (4th test session), the portion of subject contribution will be reimbursed.

8.0 Statistical Considerations

Because this is a pilot study to estimate the potential effects of sleep deprivation combined with subconcussive impacts, we are unable to identify exact sample size to accurately evaluate the combined effects, given there are no literatures to refer to. However, several studies indicate effects of sleep deprivation, as well as our previous subconcussive head impact study. Therefore, we will navigate the present study based on results from these key papers. Although we proposed here to include 10 subjects per group (a total of 40 subjects), it is important to note that we will re-evaluate effect size and disparity of data from this pilot study to propose larger-scale study, unless n=10 yields sufficient effect size with statistical meaningful results.

Effect size was calculated using the following formula:

$$S = \frac{S_1 - S_2}{2} \qquad \frac{(\bar{x}_1 - \bar{x}_2)}{\%}$$

Maruta et al. Military Med, 2014;179

Baseline vs. 26 hours post-sleep deprivation on eye movement parameters.

Tangential Error	$\frac{0.40 + 0.35}{2} = 0.375$	$\frac{0.86 - 0.63}{0.375} = 0.6133$
Radial Error	$\frac{0.74 + 0.87}{2} = 0.805$	$\frac{1.17 - 0.93}{0.805} = 0.30$

Heaton et al. Avi Spa Envron Med, 2014; 85: 497-

Baseline vs. 26 hours post-sleep deprivation on Military Sample

Tangential Error	$\frac{0.42 + 0.25}{2} = 0.335$	$\frac{0.87 - 0.59}{0.335} = 0.836$
Radial Error	$\frac{0.68 + 0.45}{2} = 0.565$	$\frac{1.17 - 0.80}{0.565} = 0.637$

Collectively, a large effect size of 0.6 is estimated from sleep deprivation studies comparing subjects' baseline to post-sleep deprived ocular-motor performance, with a standard deviation of 0.45. To achieve a power of 0.80 with alpha level = 0.05 for a two-sided independent samples t-test, 10 subjects per group are suggested for this pilot study (Formula on the right).

$$n = \frac{Z_{\alpha} \quad Z_{1-\beta} \quad SD}{\frac{2(1.96 + 0.8416)^2 (0.45)^2}{(0.6)^2}}$$

Effect Size

Data analysis

Data analysis will be conducted by Dr. Zhongxue Chen, associate professor of biostatistics and director of biostatistics counseling center. To maintain the purity of statistical analyses, Dr. Chen will be blinded to group assignments by simply being given the data set indicating Group (A, B, C, D). However, for our statistical model of longitudinal assessment, time points (Test 1, Test 2, Test 3, Test 4) will be revealed to Dr. Chen. Our primary interest is to identify the changes in ocular-motor and neurocognitive function after sleep deprivation combined with subconcussive head impacts. To this end, a series of mixed effects regression models (MRM) with random intercept will be used for all aims.[78] The first MRM will focus on the within-group pattern of changes in ocular-motor performance (smooth pursuit velocity gain, phase error, gaze position error, near point of convergence, King-Devick speed and error scores) and neurocognitive scores (complex reaction speed, verbal and working memory, exective learning) in 4 groups across the duration of the study and 4 time points. Secondly, the combination effects sleep deprivation and subconcussion will be revealed by a secondary MRM focusing on between-group analyses at each time point. Variables included in the analysis will be Group (control, subconcussion, sleep deprivation, sleep deprivation with subconcussion) and dummy variables for each time point (0 = Test 1; 1 = Test 2; 2 = Test 3; 3 = Test 4), and all two-way interactions (Group x Test 1; Group x Test 2; Group x Test 3; and Group x Test 4). The Group x Time points interactions will be the primary interest of the second MRM. All MRM models will be analyzed with Statistical Analysis System (SAS; v.9.4 for Windows, SAS) and significance level will be set at $p < 0.05$.

Study Endpoints

Throughout the study, we set the study endpoints based on subjects' well-being measured via a verbal claim to researchers. Due to the mild nature of head impact, we expect to observe a subtle change in our sensitive outcome variables after soccer headers. Additionally, when soccer heading is combined with sleep deprivation, we will make sure to frequently check subjects' statuses, and the subjects are notified researchers to terminate or pause the study procedure anytime they feel adverse symptoms. To date, there is virtually no scientific evidence available to set study endpoints using ocular-motor and neurocognitive function. Thus, we will guide the study based on symptoms, meaning that if a subject experiences any concussion-related symptoms following sleep deprivation, soccer heading, ocular-motor testing, and neurocognitive measurement, his or her participation will be terminated.

When a subject experiences any symptoms related to concussion (headache, nausea, blurred vision, disorientation, fogginess, sensitivity to light and noise, etc.), his/her participation will be terminated. However, there has not been a participant thus far who has reported concussion-related symptoms due to soccer heading, partial sleep deprivation, ocular-motor performance, and neurocognitive assessments.

9.0 Privacy/Confidentiality Issues

All participant information, and even the fact that an individual is in the study, is considered confidential. Confidentiality will be assured in this study through several mechanisms. During interviews and treatments, the investigators and study coordinator will ensure physical privacy by conducting interviews in a closed room. Subjects will be assigned a subject number to help make data anonymous. The participant's Protected Health Information will be used for research

purposes only. No names will accompany any data that is used for publication. To reduce the risk of confidentiality loss, electric data collected during the study will be stored on the university server and data collection sheets will be stored in a locked file cabinet in a locked room. The data will be stored indefinitely for data quality purpose for potential investigation after publishing the data. Only study personnel will have access to the data. All members of the research team are certified through the CITI program. Individual subject results will not be shared with the participants or their agents. Data analysis and publication will not include any identifying information.

Data Management

For ocular-motor and neurocognitive functions, we will first obtain these parameters in a data collection form (attached). Then, we will transfer these data into a RED CAP (Research Electronic Data Capture) to organize data and store. We will run a statistical analysis using Statistical Analysis System (SAS), which can identify outlier and appropriate range for acquired data.

10.0 Follow-up and Record Retention

Since we propose to include a total of 40 subjects in the study, we estimate data collection and primary analysis of 40 subjects will last approximately 15 months. The electric data collected during the study will be stored on the university server, and data collection sheets will be stored in a locked file cabinet in a locked room. The data will be stored indefinitely for data quality purpose for potential investigation after publishing the data.

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DATA PROCEDURES FORM

1. This study will gain IRB approval.
2. Recruitment

   A listserv email, describing the purpose of the study and the inclusion, exclusion, risks, and compensation involved with the study, will be sent to the students of the Indiana University School of Public Health. Flyers describing the purpose and inclusion, exclusion, risks, compensation, and contact information will be posted around the School of Public Health.
3. Interested individuals contact Sarah Coon (CoonS@Indiana.edu).

   Sarah Coon and the interested participant will set a meeting time to discuss the study in person. All meetings will be held in the School of Public Health.
4. Potential participants meet with Sarah Coon to discuss project and ask further questions.

   During this in-person meeting, the details of the study methods will be explained. The potential participant will be questioned regarding the inclusion and exclusion criteria. Should he/she meet these criteria, Coon will review the potential risks of study participation. If the potential participant does not meet the inclusion/exclusion criteria, he/she will be thanked for their interest and politely dismissed from the study with justified reasoning. Time will be allotted to thoroughly answer any questions and address any concerns the potential participants may have.
5. Participants take informed consent form with them and return with signature if they are willing to participate in the study.

   The individuals who agree to participate in the study will review the informed consent document with Coon. He/she may give their signature of consent during the meeting, or return a signed document at a later time if they wish to think about it more. Once the informed consent document is signed, the individual qualifies as a participant.
6. Participants will be randomly assigned to a group.

   Using a double sided coin and 2 coin flips, the participant will be assigned to the (a) control group, (b) sleep deprivation group, (c) subconcussion (head impact) group, or (d) sleep deprivation with subconcussion group.
7. Schedule an experiment date.

   The participant and Coon will schedule the best available dates to complete the 2-day study. The schedule will be different for the control and the subconcussion groups comparted to the sleep deprivation and sleep deprivation with subconcussion groups since the later 2 groups will complete the sleep deprivation protocol.
8. Participants fitted with ActiGraph and begin recording sleep log.

   All participants are fitted with an ActiGraph on his/her wrist 7 days prior to the start of data collection. The ActiGraph will monitor activity levels; specifically, for this study, durations of sleep. Additionally, participants will be asked to manually log their sleep hours as well as alcohol and caffeine consumption (Appendix B).
9. Test 1

Test 1 will take place on Day 1 at 08.00 and will be completed by participants in all 4 groups. In a random order, the participants will complete the following ocular-motor assessments:

i. King-Devick Test

The participant will be comfortably seated in a dim room and have his/her elbows/forearms propped against a table. He/she will hold the hand-held tablet in a comfortable fashion as to optimize his/her ability to read the screen. A researcher will instruct the participant to read aloud quickly and accurately the numbers on the screen from left to right and top to bottom; and to refrain from using any reading guides such as a finger to follow the numbers. A demonstration card will be used to model the test cards. The participant will tap the screen to begin and end each test card. One researcher will measure and record the time the participant requires to complete each of 3 test cards while another researcher will track and record any errors for each card.

ii. Eye-Sync

The Eye-Sync modality is a hand-held goggle which the participant will hold against his/her face while resting his/her elbows on a desk. The participant will be instructed to open his/her eyes as widely as possible during the nine-point calibration and the testing. The researcher will prompt the participant to keep his/her eyes open throughout the test if need be. The participant will track a projected target through six clockwise circles twice. Once the test is completed, the researcher will save and record the data.

iii. Near Point of Convergence

The near point of convergence test will be completed with the researcher and participant seated and facing perpendicular to one another. The researcher will set the target at twenty centimeters on an accommodative ruler and place the “0” end of the ruler comfortably above the participant’s upper lip. The participant will be instructed to focus on the “N” and to alert the research when the diplopia. At a rate of 1-2cm per second, the researcher will slide the target closer to the participant, stopping when the participant verbally cues the researcher or when the researcher observes mal-alignment in the participant’s eyes. The measurement will be recorded and the test will be taken twice. The average result of the 2 tests will also be calculated and recorded.

10. Participants are instructed to remain awake, not to consume caffeine (i.e. coffee, soda, tea), and to return in 12 hours.

After Test 1, all participants will be instructed not to consume caffeine and to remain awake until the next test. The ActiGraph fitness trackers will objectively report the activity level of the participant and, thus, any sleep during the day. Participants will be instructed to return for Test 2 at 20.00 on Day 1.

11. Preparation for the Sleep Deprivation Protocol

In preparation for participants to complete the sleep deprivation protocol, researchers will outfit the sleep lab. This process includes cleaning the lab; putting sheets, blankets, and pillows on the beds; and covering the motion detector for the lights. Also, instructions will be given to participants in the sleep deprivation and sleep deprivation with subconcussion groups to bring comfortable clothing and personal items with them to Test 2 as they should not leave until after Test 4 on Day 2.

12. Test 2

Test 2 will take place on Day 1 at 20.00 and will be completed by participants in all 4 groups. In a random order, the participants will complete the following ocular-motor assessments:

i. King-Devick Test

The participant will be comfortably seated in a dim room and have his/her elbows/forearms propped against a table. He/she will hold the hand-held tablet in a comfortable fashion as to optimize his/her ability to read the screen. A researcher will instruct the participant to read aloud quickly and accurately the numbers on the screen from left to right and top to bottom; and to refrain from using any reading guides such as a finger to follow the numbers. A demonstration card will be used to model the test cards. The participant will tap the screen to begin and end each test card. One researcher will measure and record the time the participant requires to complete each of 3 test cards while another researcher will track and record any errors for each card.

ii. Eye-Sync

The Eye-Sync modality is a hand-held goggle which the participant will hold against his/her face while resting his/her elbows on a desk. The participant will be instructed to open his/her eyes as widely as possible during the nine-point calibration and the testing. The researcher will prompt the participant to keep his/her eyes open throughout the test if need be. The participant will track a projected target through six clockwise circles twice. Once the test is completed, the researcher will save and record the data.

iii. Near Point of Convergence

The near point of convergence test will be completed with the researcher and participant seated and facing perpendicular to one another. The researcher will set the target at twenty centimeters on an accommodative ruler and place the “0” end of the ruler comfortably above the participant’s upper lip. The participant will be instructed to focus on the “N” and to alert the research when the “N” becomes blurry. At a rate of 1-2cm per second, the researcher will slide the target closer to the participant, stopping when the participant verbally cues the researcher or when the researcher observes mal-alignment in the participant’s eyes. The measurement will be recorded and the test will be taken twice. The average result of the 2 tests will also be calculated and recorded.

13. Sleep Deprivation Protocol

Participants in the control group and subconcussion group are instructed to sleep normally (7-9 hours), to avoid caffeine and alcohol, and to return at 07.30 on Day 2. Participants in the sleep deprivation group and the sleep deprivation with subconcussion group are shown to the prepared sleep lab to complete the sleep deprivation protocol. From the end of Test 2 until 03.00 on Day 2, when they are allowed to sleep, participants may engage in sedentary activities such as watching movies, reading, playing video games, and do light walking around the sleep lab. The researchers will monitor the participants' activity to ensure wakefulness. Snacks will be provided and water may be accessed *ad libitum.* At 03.00 the researcher will instruct the participants to go to sleep, turn off the light, and leave the lab.

14. Test 3

Test 3 will take place on Day 2 at 07.30 and will be completed by participants in all 4 groups. In a random order, the participants will complete the following ocular-motor assessments:

i. King-Devick Test

The participant will be comfortably seated in a dim room and have his/her elbows/forearms propped against a table. He/she will hold the hand-held tablet in a comfortable fashion as to optimize his/her ability to read the screen. A researcher will instruct the participant to read aloud quickly and accurately the numbers on the screen from left to right and top to bottom; and to refrain from using any reading guides such as a finger to follow the numbers. A demonstration card will be used to model the test cards. The participant will tap the screen to begin and end each test card. One researcher will measure and record the time the participant requires to complete each of 3 test cards while another researcher will track and record any errors for each card.

ii. Eye-Sync

The Eye-Sync modality is a hand-held goggle which the participant will hold against his/her face while resting his/her elbows on a desk. The participant will be instructed to open his/her eyes as widely as possible during the nine-point calibration and the testing. The researcher will prompt the participant to keep his/her eyes open throughout the test if need be. The participant will track a projected target through six clockwise circles twice. Once the test is completed, the researcher will save and record the data.

iii. Near Point of Convergence

The near point of convergence test will be completed with the researcher and participant seated and facing perpendicular to one another. The researcher will set the target at twenty centimeters on an accommodative ruler and place the "0" end of the ruler comfortably above the participant's upper lip. The participant will be instructed to focus on the "N" and to alert the research when the "N" becomes blurry. At a rate of 1-2cm per second, the researcher

will slide the target closer to the participant, stopping when the participant verbally cues the researcher or when the researcher observes mal-alignment in the participant's eyes. The measurement will be recorded and the test will be taken twice. The average result of the 2 tests will also be calculated and recorded.

15. Soccer Intervention preparation

    The JUGS machine will be turned on and speed will be set to 25mph. A tape mark will be placed 40 feet from the JUGS machine to indicate where participants should stand.

16. Soccer Intervention

    Participants in the sleep deprivation with subconcussion and subconcussion groups will complete the Soccer Intervention. While the participant stands 40 meters away from the JUGS machine, it will launch a standard soccer ball will be at him/her at a speed of 25 miles per hour. The participant will return the soccer ball toward the machine by heading the ball. This will be repeated at a cadence of 1 header per minute for ten minutes. Participants in the control and sleep deprivation groups will kick the ball, traveling 25 miles per hour, at a cadence of 1 per minute for ten minutes.

17. Test 4

    Test 4 will take place on Day 2 at 08.15 and will be completed by participants in all 4 groups. In a random order, the participants will complete the following ocular-motor assessments:

    i. King-Devick Test

       The participant will be comfortably seated in a dim room and have his/her elbows/forearms propped against a table. He/she will hold the hand-held tablet in a comfortable fashion as to optimize his/her ability to read the screen. A researcher will instruct the participant to read aloud quickly and accurately the numbers on the screen from left to right and top to bottom; and to refrain from using any reading guides such as a finger to follow the numbers. A demonstration card will be used to model the test cards. The participant will tap the screen to begin and end each test card. One researcher will measure and record the time the participant requires to complete each of 3 test cards while another researcher will track and record any errors for each card.

    ii. Eye-Sync

       The Eye-Sync modality is a hand-held goggle which the participant will hold against his/her face while resting his/her elbows on a desk. The participant will be instructed to open his/her eyes as widely as possible during the nine-point calibration and the testing. The researcher will prompt the participant to keep his/her eyes open throughout the test if need be. The participant will track a projected target through six clockwise circles twice. Once the test is completed, the researcher will save and record the data.

    iii. Near Point of Convergence

The near point of convergence test will be completed with the researcher and participant seated and facing perpendicular to one another. The researcher will set the target at twenty centimeters on an accommodative ruler and place the “0” end of the ruler comfortably above the participant’s upper lip. The participant will be instructed to focus on the “N” and to alert the research when the “N” becomes blurry. At a rate of 1-2cm per second, the researcher will slide the target closer to the participant, stopping when the participant verbally cues the researcher or when the researcher observes mal-alignment in the participant’s eyes. The measurement will be recorded and the test will be taken twice. The average result of the 2 tests will also be calculated and recorded.

18. Compensation

Compensation for time will be provided to the participants. Participants who underwent the sleep deprivation protocol (sleep deprivation group and sleep deprivation with subconcussion group) will receive $80 while those in the control and subconcussive head impact groups will be compensated $30. Any participant who does not complete the entire research will be compensated a prorated amount.

APPENDIX D:

DATA COLLECTION FORM & SURVEY

INDIANA UNIVERSITY INFORMED CONSENT STATEMENT

Acute effects of sleep deprivation and subconcussive impact on ocular-motor function and neurocognitive function

You are invited to participate in a research study using tools to detect eye movement and brain function after partial sleep deprivation and/or soccer heading. You are selected as a possible subject because you are a current member of a soccer team who is 18-26 years old and have at least 5 years of soccer heading experience. Please read this form and ask any questions you may have before agreeing to be in the study.

The study is being conducted by Keisuke Kawata, PhD, ATC, Sarah Coon, BS., ATC, Indiana University Department of Kinesiology: Zhongxue Chen, PhD, Department of Epidemiology and Biostatistics, Sharlene Newman, PhD, Department of Psychological and Brain Sciences

STUDY PURPOSE
Often, athletes find themselves competing or practicing sport having slept less than the recommended time of 7-9 hours per night. Athletes often receive head impacts like soccer headings that may not cause them to show symptoms such as headache, confusion, and dizziness. These impacts are referred as subconcussive impacts. Tracking eye-movements allows researchers objective insight to brain function. To this day, we do not know the combined effects of sleep deprivation and sub-concussive head impacts have on ocular-motor and neurocognitive functions. The purpose of this study is to examine if sleep deprivation, subconcussive impacts, or a combination of both changes eye-movements and neurocognitive function.

NUMBER OF PEOPLE TAKING PART IN THE STUDY
If you agree to participate, you will be one of 40 subjects who will be participating in this research. We plan to recruit 40 soccer players.

PROCEDURES FOR THE STUDY
For soccer players, if you agree to be in the study, you will be randomly assigned to either a control, sleep deprivation, soccer heading, or sleep deprivation with soccer heading group.

The study consists of 4 test sessions during a 2-day period. Each test session will be approximately 30 minutes in length. Based on your group assignment, you will participate in 1) partial sleep deprivation or regular sleep, and 2) soccer heading or soccer kicking.
1 week prior to the study, we will ask you to log your sleep schedule.
48 hours prior to the Test 1 you must refrain from consuming alcohol.
On the 1st day of the study, you must refrain from consuming caffeine.
After Test 1 (7am Day 1), you must refrain from sleeping during the day
You will come back to the lab for Test 2 (8pm Day 1)
After Test 2,
the sleep deprivation group and the sleep deprivation & soccer heading groups stay in the lab and sleep from 2am – 6am on Day 2.
the control and soccer heading groups sleep normally (10p-6a)
Test 3 will take place for all groups at 8am of Day 2.
After Test 3,

the soccer heading group and the sleep deprivation & soccer heading groups will perform soccer heading
the sleep deprivation group and control group will perform soccer kicking
Test 4 will take place after soccer heading or kicking.

During each test session you will complete the same tests: smooth pursuit, a near-point of convergence test, King Devick test, and an ImPACT neurocognitive test. The smoot pursuit test is a virtual reality modality that records your eye movement as you track a moving target on the screen. The near-point of convergence test is measuring how close an object can be to your nose before it becomes blurry. The King-Devick test is a timed reading test. The ImPACT test is a computer-based neurocognitive function test that is currently used clinically as a diagnostic tool for concussions.

Between Test 3 and Test 4, you will perform either soccer heading (soccer heading group and sleep deprivation & soccer heading group), or kicking (sleep deprivation group and control group). A standard size 5 soccer ball will be projected at 25 mph (equivalent speed to a long throw-in) by a JUGS soccer machine, and you will perform 10 headers or 10 kicks, depending on what group you are assigned to. You will have a 1 min rest between each performance.

RISKS OF TAKING PART IN THE STUDY

While on the study, the risks are:

During soccer heading there is a risk of an injury to your face such as laceration, broken nose, or bruising. There is also a risk of eye, nose, or mouth injury. You may experience minimal transient muscle or joint soreness because of the soccer heading. There is a low risk of concussion and experiencing 1 or more concussion-related symptoms during soccer heading. However, as a soccer player, this type of heading task is a fundamental skill, and you are probably regularly performing the headers during practices and games. We believe the risk is low because most of the previous research did not show any facial injury or concussion-related symptoms. If you are diagnosed with a concussion it will disqualify you from participating in future sporting events until you can safely return to play as determined by a physician. If a diagnostic test (such as a CT scan) is needed, it is not part of the research, but rather part of the clinical management possibly suggested by your physician.

After sleep deprivation, you may feel drowsy, confused, fatigue, blurred vision, and/or disoriented. You may experience a headache and difficulty concentrating. Multiple studies show that these symptoms will reverse themselves after 1 night of recovery sleep. If symptoms do not resolve, please contact your physician for further medical attention.

While you are performing eye movement tasks, you may experience a headache or dizziness. The test lasts 30 seconds, and you are free to stop whenever you feel any symptoms.

BENEFITS OF TAKING PART IN THE STUDY

You are not expected to directly benefit from this research, however, as a result of this work we will advance our knowledge regarding the effects of mild head impacts. The proposed study is to identify and understand the effect of sleep deprivation and soccer heading on eye movements. This work is one of the first steps to unravel public health concern in concussion and subconcussion, using safe and state-of-the-art methodologies.

CONFIDENTIALITY

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Your identity will be held in confidence in reports in which the study may be published and data will be stored in the Indiana University online server, and data collection sheets will be stored in a locked file cabinet in a locked room.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the Indiana University Institutional Review Board or its designees, and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP) who may need to access your research records.

COSTS

Taking part in this study may lead to added costs to you or your insurance company. If you experience concussion-related symptoms, you or your insurance company will be responsible for the following costs: doctor's office visit, medications, and neuroimaging. You will not be responsible for any of study-specific costs.

PAYMENT

You will receive payment for taking part in this study. Regardless of the group assignment, you will receive $70 at the end of Test session 4 (Day 2). If you are unable to advance beyond Test 1, albeit sleep duration, voluntary dropout, change in schedule, then your compensation will be prorated.

COMPENSATION FOR INJURY

In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled. If you are participating in research that is not conducted at a medical facility, you will be responsible for seeking medical care and for the expenses associated with any care received.

CONTACTS FOR QUESTIONS OR PROBLEMS

For questions about the study or a research-related injury, contact the researcher, Keisuke Kawata, PhD at 812-855-5244. If you cannot reach the researcher during regular business hours (i.e., 8 a.m. to 5 p.m.), please call the IU Human Subjects Office at 812-856-4242 or 800-696-2949. After business hours, please call Keisuke Kawata, PhD at 870-210-9918.

In the event of an emergency, you may contact Keisuke Kawata, PhD, at 870-210-9918.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or offer input, contact the IU Human Subjects Office at 812-856-4242 or 800-696-2949.

VOLUNTARY NATURE OF THIS STUDY

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your decision whether or not to participate in this study will not affect your current or future relations with Indiana University.

Your participation may be terminated by the investigator without regard to your consent in the following circumstances: you elicit visible disorientation due to the heading protocol or any of measurements. It is to ensure safety for you and research environment.

SUBJECT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study.

I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Subject's Printed Name: _____

Subject's Signature:
_____Date:_____
(must be dated by the subject)

Printed Name of Person Obtaining Consent: _____

Signature of Person Obtaining Consent:
_____Date:_____

HEALTH AND CONCUSSION HISTORY QUESTIONNAIRE

Subject Number_____ Date_____

Please answer the following questions honestly and to the best of your ability.

1. **Age ____**

Height ____

Weight ____

2. Are you a current member of a soccer team? YES ___ NO_ __

2a. What level? Collegiate ___ Club ___ Recreation___ Professional___

3. How long have you a. played soccer? ____ yrs **b. been soccer heading?** ____ yrs

4. Have you ever been diagnosed by a certified athletic trainer or physician with a concussion? YES ___ NO_ __

4b. For your concussion(s), approximately when did the concussion(s) occur, how long did signs and symptoms last, and how long did you miss athletic participation (please list per concussion, use back of paper if necessary)?

Concussion	Date (month-year)	Signs and Symptoms Duration (# of days)	Length of time until you returned to practice or game (# of days)
1			
2			
3			
4			
5			

5. Please circle yes or no to the following and explain as needed.

YES NO Have you had any head, neck, or face injury in the 1 year prior to the study?
If yes, then please explain.

YES NO Do you have a history of vestibular dysfunction (e.g., vertigo)?
If yes, then please explain.

YES NO Do you have a history of hearing dysfunction (e.g., deafness)?
If yes, then please explain.

YES NO Do you have a history of vision problems (e.g., macular degeneration)?
If yes, then please explain.

YES NO Do you need corrective eyewear? (glasses or contacts)?

YES NO If yes, would you be able to wear contacts during testing

YES NO Are you *currently* taking any medications affecting balance (e.g., antibiotics)?
If yes, then please explain.

YES NO Have you had any lower extremity injuries in the past 1 year?
If yes, then please explain.

YES NO Are you currently pregnant?

YES NO Do you have a metal implants (e.g., pacemaker, ferromagnetic aneurysm clip)?
If yes, then please explain.

YES NO Do you have any neurological disorders (e.g., seizure disorders, closed head injuries with loss of consciousness greater than 15 minutes, CNS neoplasm, history of stroke)?

If yes, then please explain.

YES NO Do you have hypertension, cardiac arrhythmia, or pulmonary disease?
If yes, then please explain.

TAKE HOME INSTRUCTIONS

Date_____

Dear Participant,

Today you were fitted with an ActiGraph monitor. While this fitness tracker will monitor all activity levels, we are primarily looking at quantity of sleep. If the tracker shows less than an average of 7-9hours per night, you will be excluded from the study.

Below are instructions on what you should do between now and Test 1:

- **Wear this tracker all week.** It does not have to be pressed to your skin, but should not be loose or floppy around your wrist.

- The device is water proof. However, if you prefer to remove it when showering or engaging in other water activities that is fine, we just ask that you return it to your wrist promptly after drying off.

- **Fill out the sleep log** each night and morning with the date, time going to bed, time waking up, and information of caffeine/alcohol consumption.

- **Return the completed sleep log and ActiGraph monitor** on the first day of testing which will be _____ at 7:00 am.

If you have any questions or concerns, please do not hesitate to contact me, Sarah Coon, via email (CoonS@indiana.edu) or phone (336-580-2627).

Thank you for participating in our study!

Sarah Coon, LAT, ATC
Indiana University
Master's Candidate
Post-Professional Athletic Training Program

Sleep log
Subject Number _____

Sleep Log

Date							
I went to bed at…. (time)	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM
I fell asleep at…. (time) *complete next morning*	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM
I woke up at… (time) *complete next morning*	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM
I got out of bed at…. (time) *complete next morning*	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM
I woke up during the night (# times)							
Number of caffeine drinks today (#)							
Last time of caffeine drinks today (time)	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM
Number of alcoholic drinks today (#)							
Last time of alcoholic drinks today (time)	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM	AM/PM

We do not encourage the removal of the activity tracker for any period of time. However, if you do take it off, please record the date & the time it was taken off and replaced here: _____
_____
_____
_____

DATA COLLECTION FORM

Subject #_____ Sex (M / F) Age ____ Height ____ Weight ____

Soccer Heading Head Kinematics Assessment

Variable	1	2	3	4	5	6	7	8	9	10	Sum	Average
Peak Linear acc												
Peak Angular acc												
HIC												
GSI												

Assessment		Trial / Measure		Test 1	Test 2	Test 3	Test 4
Ocular-Motor	King-Devick	Card 1	Time				
			Errors				
		Card 2	Time				
			Errors				
		Card 3	Time				
			Errors				
		Total	Time				
			Errors				
	NPC	Trail 1	Centimeters				
		Trial 2	Centimeters				
		Average	Centimeters				
	EYE-SYNC	Reliability Color					
		Tangential Variability					
		Radial Variability					
		Mean Phase Error					
		Mean Radial Error					
		Horizontal Gain					
		Vertical Gain					
Neurocognitive Function	ImPACT Test	Verbal Memory					
		Visual Memory					
		Visual Motor Speed					
		Reaction Time					
		Impulse Control					
		Symptom Score					

APPENDIX E:

RAW DATA TABLES

Subject Number	Sleep Dep 1=yes 0=no	Sex	Age	Average Sleep (Min)	Sleep Intervention (Min)	KD 1 Total Time (Sec)	KD 2 Total Time (Sec)	KD 3 Total Time (Sec	KD 1 Total Errors	KD 2 Total Errors	KD 3 Total Errors
0001	0	0	20	427.7	402	40.5	40	39.5	2	1	0
0002	0	0	19	434.14	449	41.6	38.1	34.1	0	0	0
0010	0	1	20	350.71	435	48.7	44.5	44.3	0	0	0
0013	0	1	21	437.57	422	39.7	42.2	41	1	3	1
0016	0	0	19	496	448	43.3	38.4	36	0	0	0
0018	0	1	19	459.57	408	37.5	38.1	37.6	0	0	0
0019	0	0	20	424.71	444	43.6	40.6	37.7	1	0	0
0021	0	0	22	455.71	450	37.5	34.1	35	2	0	1
0025	0	0	22	439.57	402	49.7	47	40.1	0	0	0
0027	0	0	20	462.14	397	40.7	39.1	37.4	0	0	0
0101	0	1	23	433	405	48.7	44.3	47.6	1	0	1
0103	0	0	21	489	451	46.6	41.6	41.4	2	0	1
0104	0	0	21	469.42	417	37.9	31.6	30.5	1	0	0
0106	0	1	20	460.28	370	44.7	39.4	40	0	0	0
0108	0	1	20	499.42	462	35.6	35.6	34.5	0	1	1
0109	0	0	21	483.57	432	38.3	40	36.1	0	4	0
0110	0	0	20	441.28	315	40.5	38.8	36.8	0	0	0
0112	0	1	21	477.57	426	47.4	48.6	43.4	0	0	0
0115	0	1	19	437.28	427	36.2	37.1	32.9	0	0	0
0116	0	1	23	488.57	432	42.2	44	42.9	0	1	0
1003	1	1	21	422.28	153	39.8	37.5	37.5	0	1	1

Subject Number	Sleep Dep 1=yes 0=no	Sex	Age	Average Sleep (Min)	Sleep Intervention (Min)	KD 1 Total Time (Sec)	KD 2 Total Time (Sec)	KD 3 Total Time (Sec	KD 1 Total Errors	KD 2 Total Errors	KD 3 Total Errors
1004	1	1	21	435.57	164	55.8	52.8	54	0	0	0
1007	1	0	20	423.71	185	43.8	39.8	39.7	0	0	0
1009	1	1	18	424.85	223	39	34.8	34.4	0	1	0
1011	1	1	19	425	221	34.6	31.6	35	3	3	4
1012	1	1	20	551.28	226	44.5	44.1	45.5	0	0	0
1013	1	1	21	408.14	210	39.5	39.7	41.2	0	0	1
1014	1	1	19	470.14	215	35.4	32.2	36.5	0	0	2
1016	1	0	21	465.42	227	34.2	33	32.7	0	0	0
1018	1	0	20	499.85	231	40	35.8	37.5	0	1	0
1021	1	0	20	458.28	243	41.6	40.7	41.1	0	0	0
1101	1	1	20	486.71	171	43.4	43.1	42.6	0	0	0
1102	1	0	22	413.14	155	31.3	32.2	33.4	0	0	0
1104	1	1	20	432.71	171	43.1	40.6	40.2	0	0	0
1105	1	1	25	387.57	157	52	53.9	60.9	1	0	2
1107	1	0	20	445.85	180	38.2	36.7	41.1	0	0	0
1108	1	0	22	426.57	173	42.3	39.2	50.7	0	0	1
1111	1	0	20	520	172	43.6	39	46.8	0	0	0
1112	1	1	22	397.71	177	49.4	36.7	38.3	0	2	0
1113	1	1	21	378.14	168	37.4	32.3	30.3	0	2	0
1114	1	0	21	371.28	161	42.9	40.6	42.6	0	0	1
1115	1	0	21	412.57	159	37.2	35	37.2	0	0	0

APPENDIX F:

SPSS OUTPUT

```
GET DATA
  /TYPE=XLSX
  /FILE='\\Client\C$\Users\sgc95\Google Drive\Research\Data Collection Process\Data\Data
Collection Feb 21 2018 .xlsx'
  /SHEET=name 'Chen'
  /CELLRANGE=FULL
  /READNAMES=ON
  /DATATYPEMIN PERCENTAGE=95.0
  /HIDDEN IGNORE=YES.
EXECUTE.
DATASET NAME DataSet1 WINDOW=FRONT.
EXAMINE VARIABLES=Test1time Test2Time Test3Time BY Group
  /ID=subject#
  /PLOT BOXPLOT NPPLOT
  /COMPARE GROUPS
  /STATISTICS DESCRIPTIVES EXTREME
  /CINTERVAL 95
  /MISSING REPORT
  /NOTOTAL.
```

Explore

Notes

Output Created		26-FEB-2018 19:12:39
Comments		
Input	Active Dataset	DataSet1
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	42
Missing Value Handling	Definition of Missing	User-defined missing values for dependent variables are treated as missing. User-defined and system missing values for factors are treated as valid data.
	Cases Used	Statistics are based on cases with no missing values for any dependent variable or factor used.

Syntax		EXAMINE VARIABLES=Test1time Test2Time Test3Time BY Group /ID=subject# /PLOT BOXPLOT NPPLOT /COMPARE GROUPS /STATISTICS DESCRIPTIVES EXTREME /CINTERVAL 95 /MISSING REPORT /NOTOTAL.
Resources	Processor Time	00:00:03.22
	Elapsed Time	00:00:02.02

[DataSet1]

Group

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	Group	N	Percent	N	Percent	N	Percent
Test 1 time	Control	20	100.0%	0	0.0%	20	100.0%
	Sleep Deprivation	22	100.0%	0	0.0%	22	100.0%
Test 2 Time	Control	20	100.0%	0	0.0%	20	100.0%
	Sleep Deprivation	22	100.0%	0	0.0%	22	100.0%
Test 3 Time	Control	20	100.0%	0	0.0%	20	100.0%
	Sleep Deprivation	22	100.0%	0	0.0%	22	100.0%

Descriptives

	Group			Statistic	Std. Error
Test 1 time	Control	Mean		42.045	.9843
		95% Confidence Interval for Mean	Lower Bound	39.985	
			Upper Bound	44.105	
		5% Trimmed Mean		41.978	
		Median		41.150	
		Variance		19.377	
		Std. Deviation		4.4020	
		Minimum		35.6	
		Maximum		49.7	
		Range		14.1	
		Interquartile Range		8.1	
		Skewness		.349	.512
		Kurtosis		-1.048	.992
	Sleep Deprivation	Mean		41.318	1.2376
		95% Confidence Interval for Mean	Lower Bound	38.744	
			Upper Bound	43.892	
		5% Trimmed Mean		41.075	
		Median		40.800	
		Variance		33.697	
		Std. Deviation		5.8049	
		Minimum		31.3	
		Maximum		55.8	
		Range		24.5	
		Interquartile Range		6.3	
		Skewness		.750	.491
		Kurtosis		.877	.953
Test 2 Time	Control	Mean		40.155	.9326
		95% Confidence Interval for Mean	Lower Bound	38.203	
			Upper Bound	42.107	
		5% Trimmed Mean		40.161	
		Median		39.700	
		Variance		17.395	
		Std. Deviation		4.1708	
		Minimum		31.6	
		Maximum		48.6	
		Range		17.0	
		Interquartile Range		5.5	

		Skewness		.118	.512
		Kurtosis		.147	.992
	Sleep Deprivation	Mean		38.695	1.2718
		95% Confidence Interval for Mean	Lower Bound	36.051	
			Upper Bound	41.340	
		5% Trimmed Mean		38.247	
		Median		38.250	
		Variance		35.583	
		Std. Deviation		5.9652	
		Minimum		31.6	
		Maximum		53.9	
		Range		22.3	
		Interquartile Range		6.3	
		Skewness		1.255	.491
		Kurtosis		1.708	.953
Test 3 Time	Control	Mean		38.440	.9469
		95% Confidence Interval for Mean	Lower Bound	36.458	
			Upper Bound	40.422	
		5% Trimmed Mean		38.372	
		Median		37.650	
		Variance		17.934	
		Std. Deviation		4.2349	
		Minimum		30.5	
		Maximum		47.6	
		Range		17.1	
		Interquartile Range		6.1	
		Skewness		.265	.512
		Kurtosis		-.152	.992
	Sleep Deprivation	Mean		40.873	1.5482
		95% Confidence Interval for Mean	Lower Bound	37.653	
			Upper Bound	44.092	
		5% Trimmed Mean		40.370	
		Median		39.950	
		Variance		52.730	
		Std. Deviation		7.2615	
		Minimum		30.3	
		Maximum		60.9	
		Range		30.6	
		Interquartile Range		7.2	

	Skewness	1.192	.491
	Kurtosis	1.661	.953

Extreme Values

	Group			Case Number	subject #	Value
Test 1 time	Control	Highest	1	6	0025	49.7
			2	13	0101	48.7
			3	19	0010	48.7
			4	8	0112	47.4
			5	14	0103	46.6
		Lowest	1	17	0108	35.6
			2	4	0115	36.2
			3	3	0018	37.5
			4	2	0021	37.5
			5	15	0104	37.9
	Sleep Deprivation	Highest	1	27	1004	55.8
			2	38	1105	52.0
			3	39	1112	49.4
			4	30	1012	44.5
			5	35	1007	43.8
		Lowest	1	37	1102	31.3
			2	32	1016	34.2
			3	29	1011	34.6
			4	31	1014	35.4
			5	42	1115	37.2
Test 2 Time	Control	Highest	1	8	0112	48.6
			2	6	0025	47.0
			3	19	0010	44.5
			4	13	0101	44.3
			5	5	0116	44.0
		Lowest	1	15	0104	31.6
			2	2	0021	34.1
			3	17	0108	35.6
			4	4	0115	37.1
			5	10	0002	38.1[a]
	Sleep Deprivation	Highest	1	38	1105	53.9
			2	27	1004	52.8
			3	30	1012	44.1
			4	21	1101	43.1
			5	34	1021	40.7
		Lowest	1	29	1011	31.6
			2	37	1102	32.2

			3	31	1014	32.2
			4	40	1113	32.3
			5	32	1016	33.0
Test 3 Time	Control	Highest	1	13	0101	47.6
			2	19	0010	44.3
			3	8	0112	43.4
			4	5	0116	42.9
			5	14	0103	41.4
		Lowest	1	15	0104	30.5
			2	4	0115	32.9
			3	10	0002	34.1
			4	17	0108	34.5
			5	2	0021	35.0
	Sleep Deprivation	Highest	1	38	1105	60.9
			2	27	1004	54.0
			3	24	1108	50.7
			4	25	1111	46.8
			5	30	1012	45.5
		Lowest	1	40	1113	30.3
			2	32	1016	32.7
			3	37	1102	33.4
			4	28	1009	34.4
			5	29	1011	35.0

a. Only a partial list of cases with the value 38.1 are shown in the table of lower extremes.

Tests of Normality

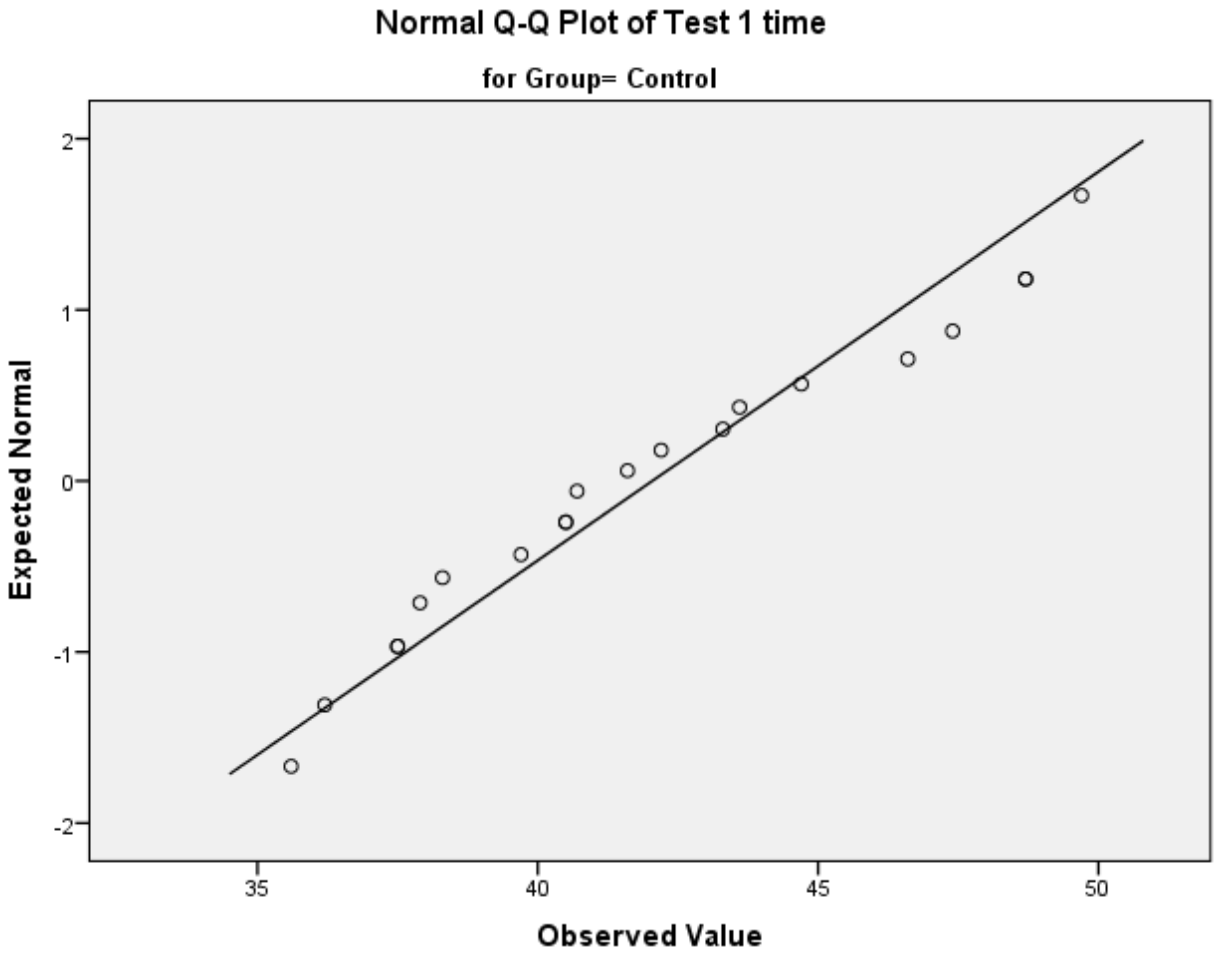
	Group	Kolmogorov-Smirnov[a] Statistic	df	Sig.	Shapiro-Wilk Statistic	df	Sig.
Test 1 time	Control	.120	20	.200*	.942	20	.263
	Sleep Deprivation	.155	22	.180	.952	22	.343
Test 2 Time	Control	.115	20	.200*	.982	20	.957
	Sleep Deprivation	.187	22	.045	.877	22	.010
Test 3 Time	Control	.119	20	.200*	.989	20	.997
	Sleep Deprivation	.179	22	.066	.918	22	.068

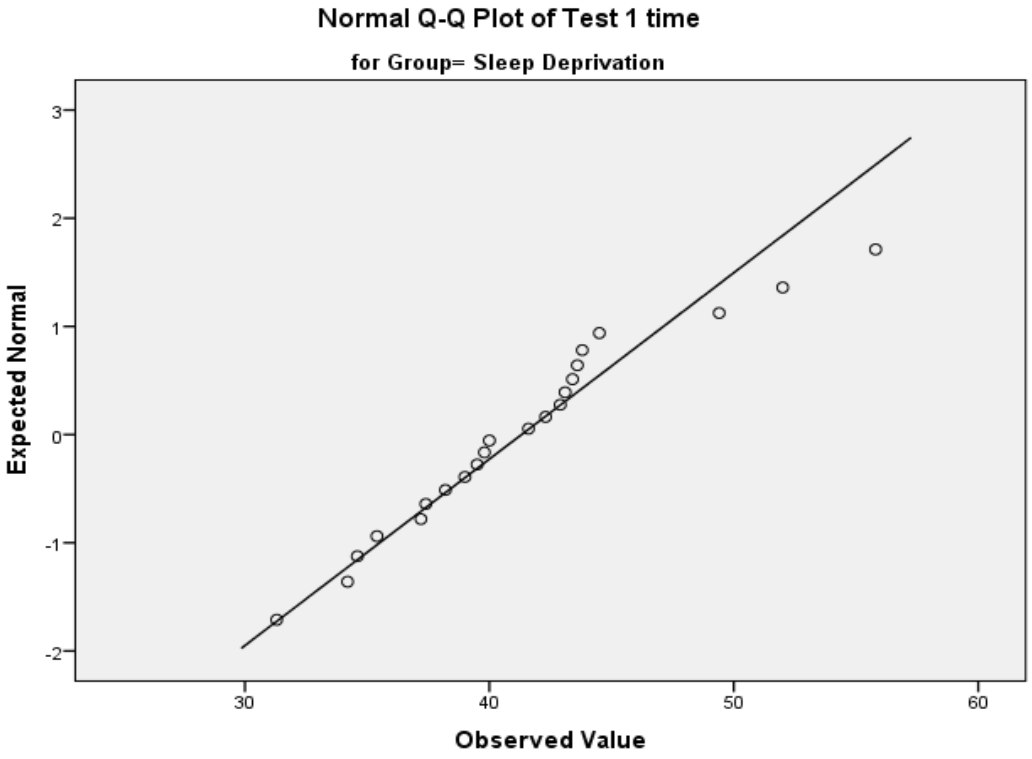
*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

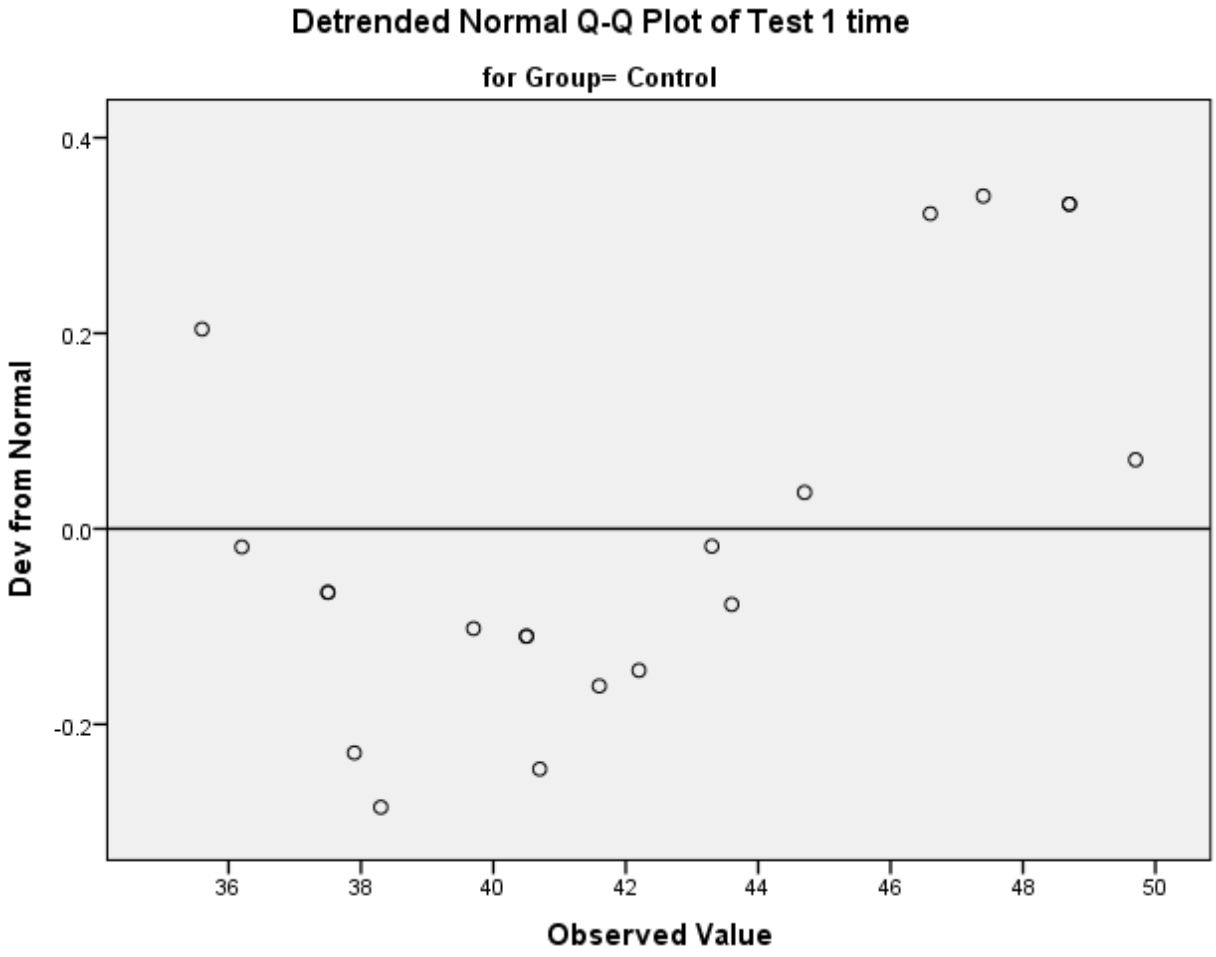
Test 1 time

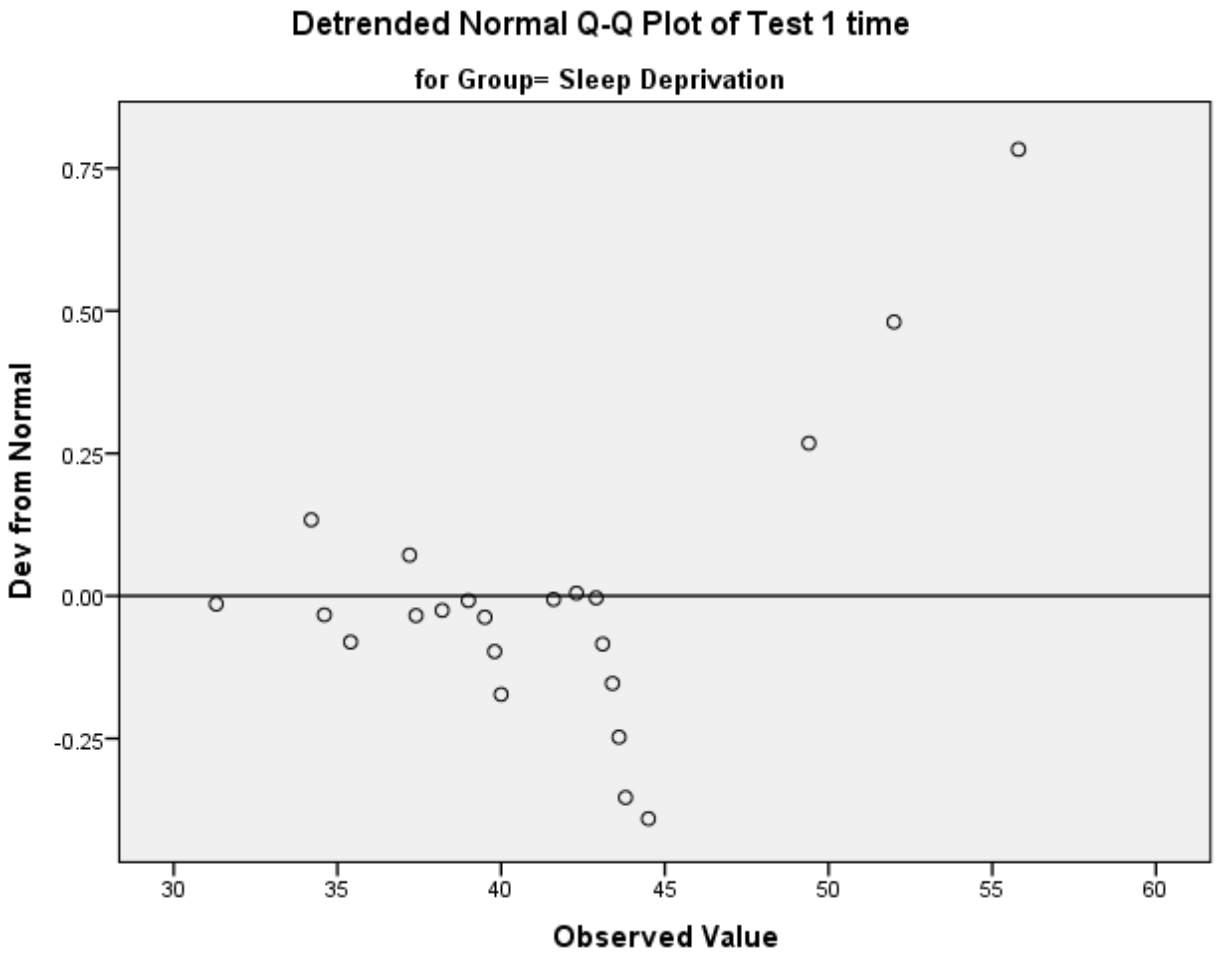
Normal Q-Q Plots

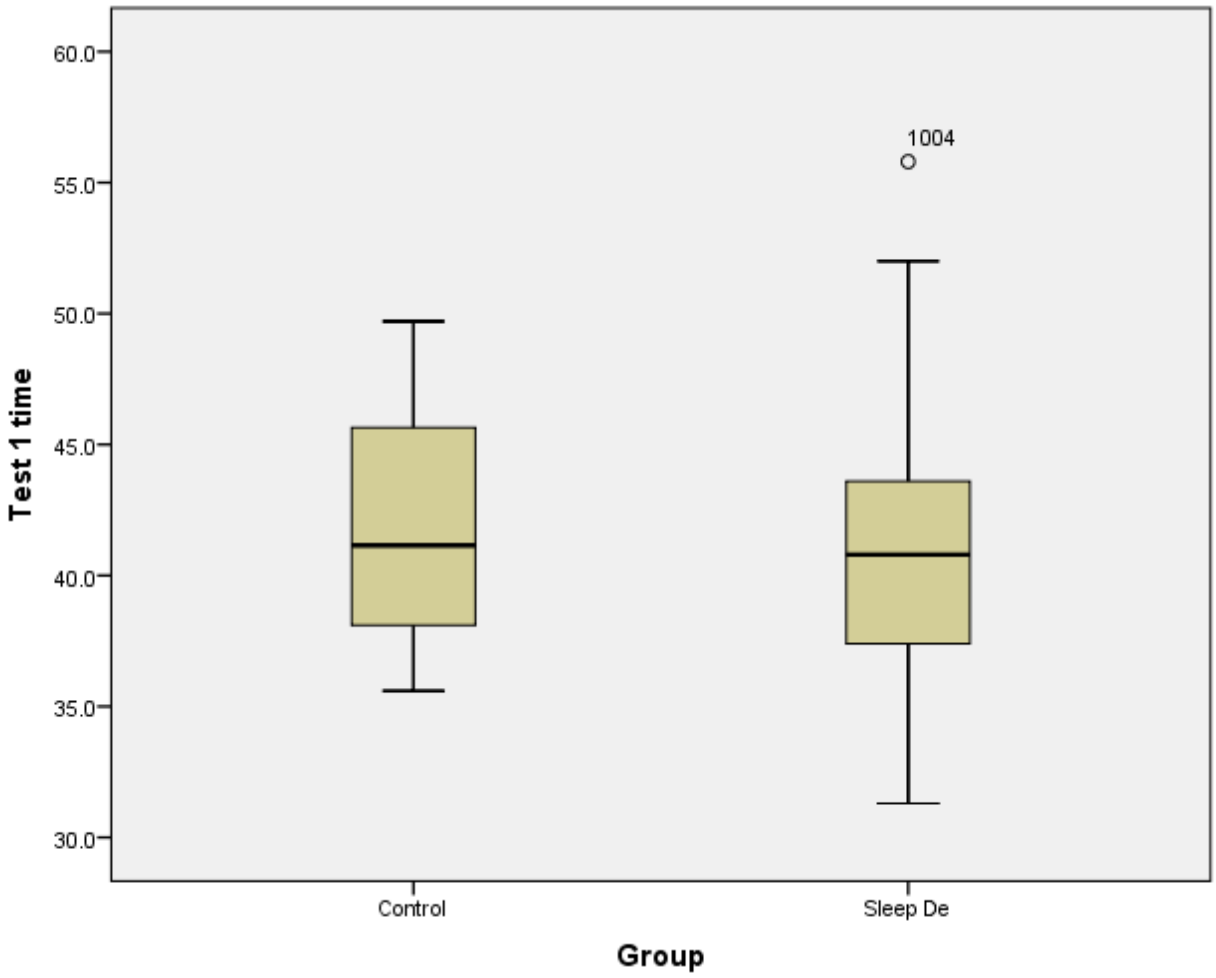



Normal Q-Q Plot of Test 1 time
for Group= Sleep Deprivation
Expected Normal
Observed Value
3
2
1
0
-1
-2
30
40
50
60

Detrended Normal Q-Q Plots

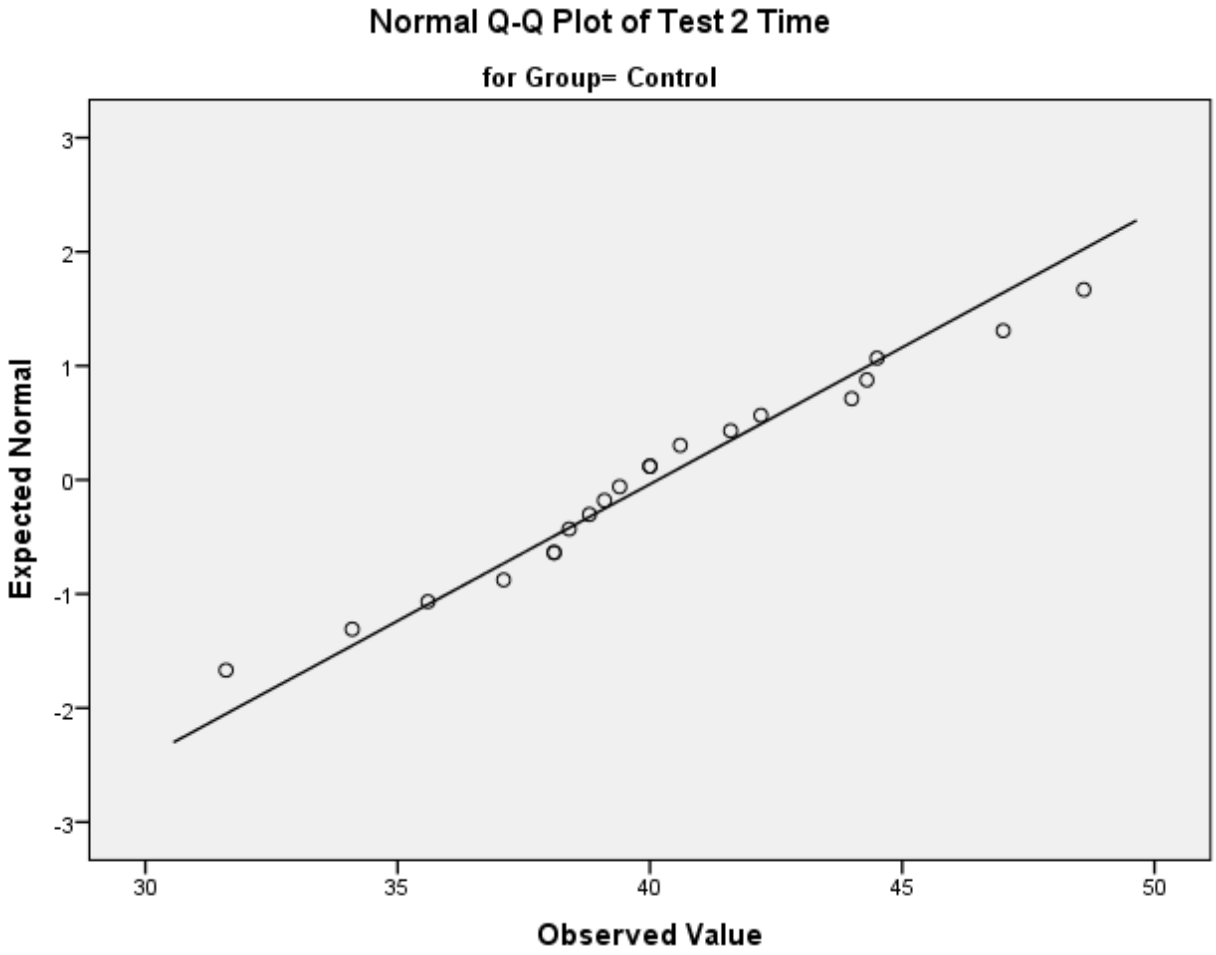


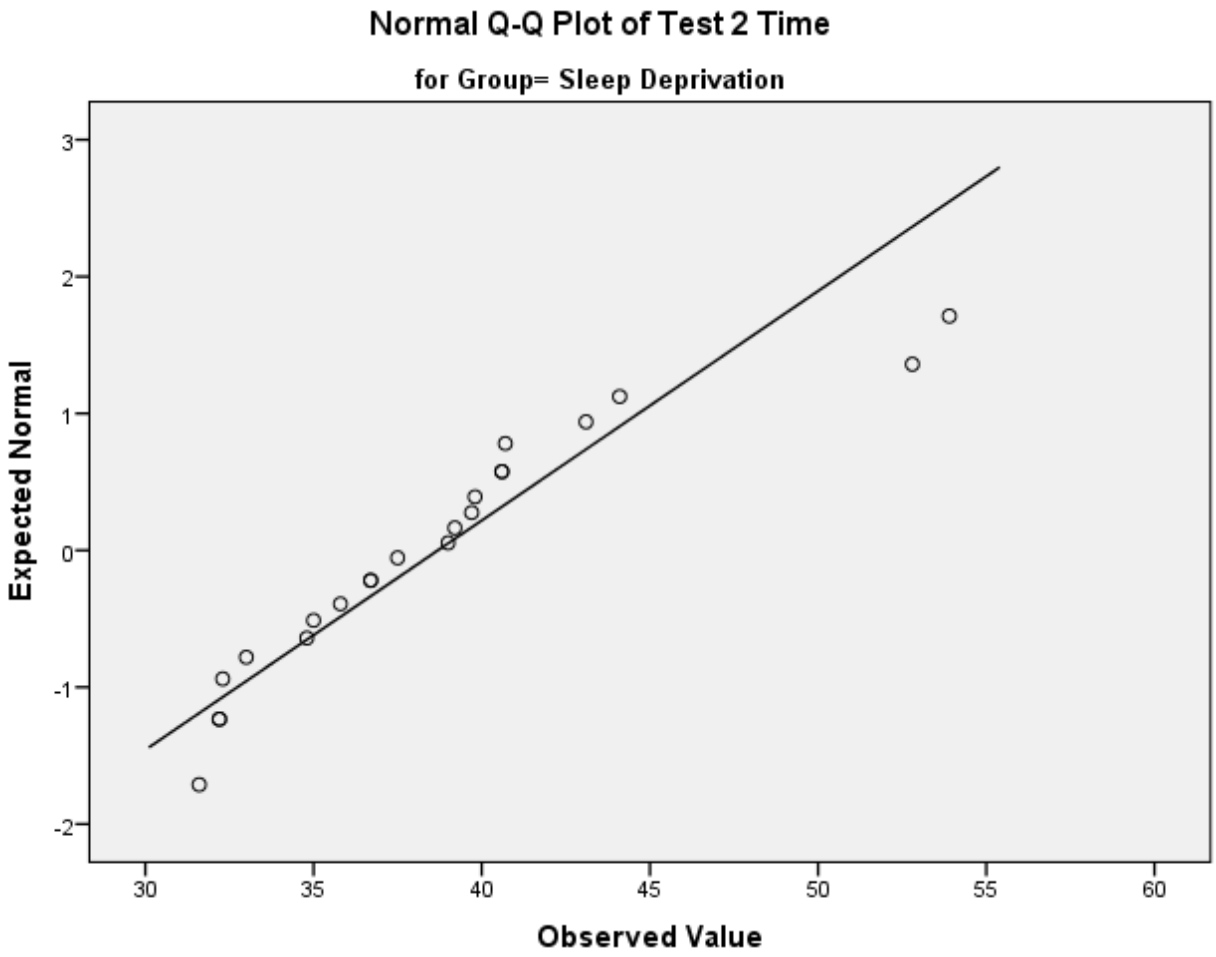

Detrended Normal Q-Q Plot of Test 1 time
for Group= Sleep Deprivation
Dev from Normal
0.75
0.50
0.25
0.00
-0.25
30
35
40
45
50
55
60
Observed Value


60.0
55.0
50.0
45.0
40.0
35.0
30.0
Test 1 time
1004
Control
Sleep De
Group

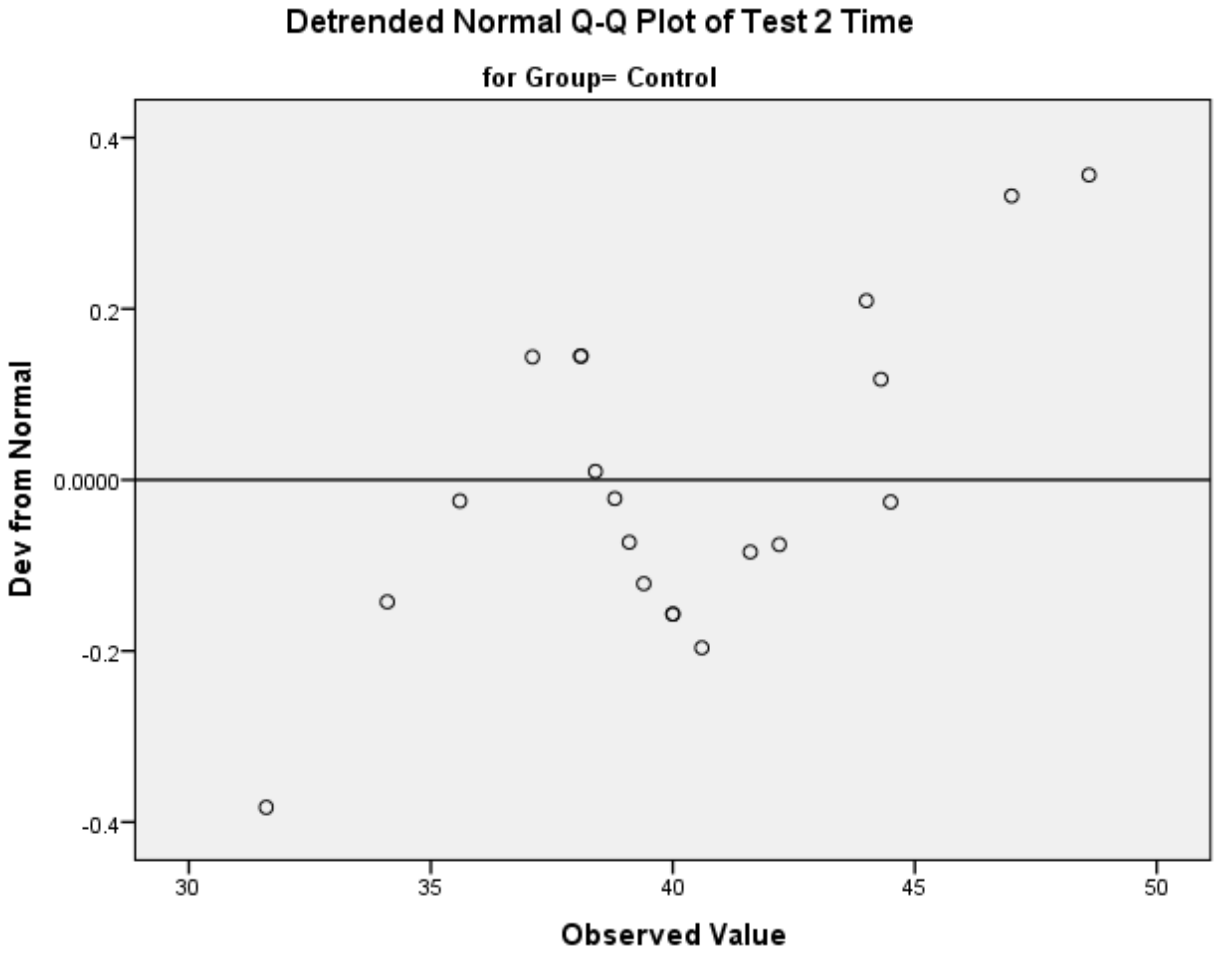
Test 2 Time

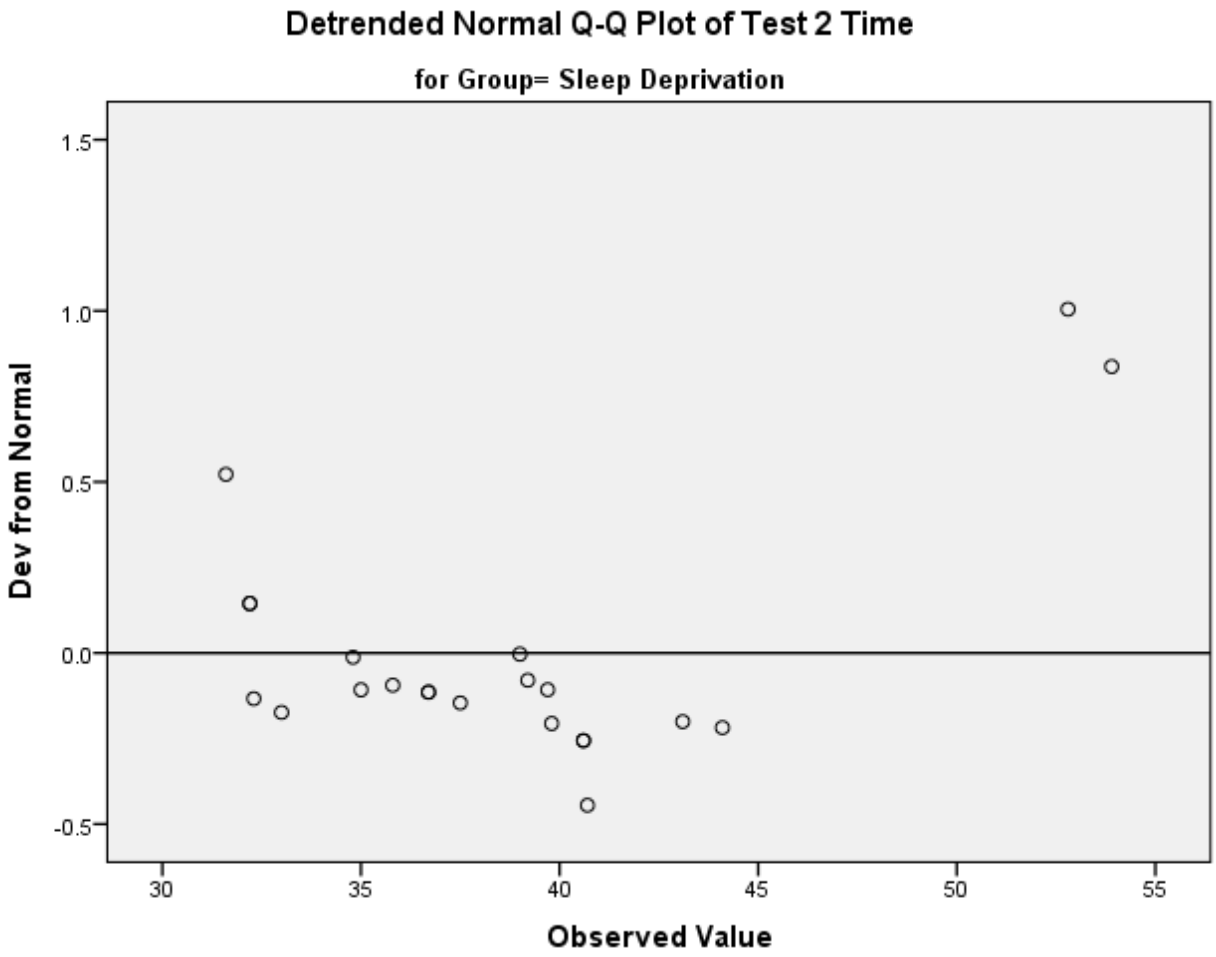
Normal Q-Q Plots

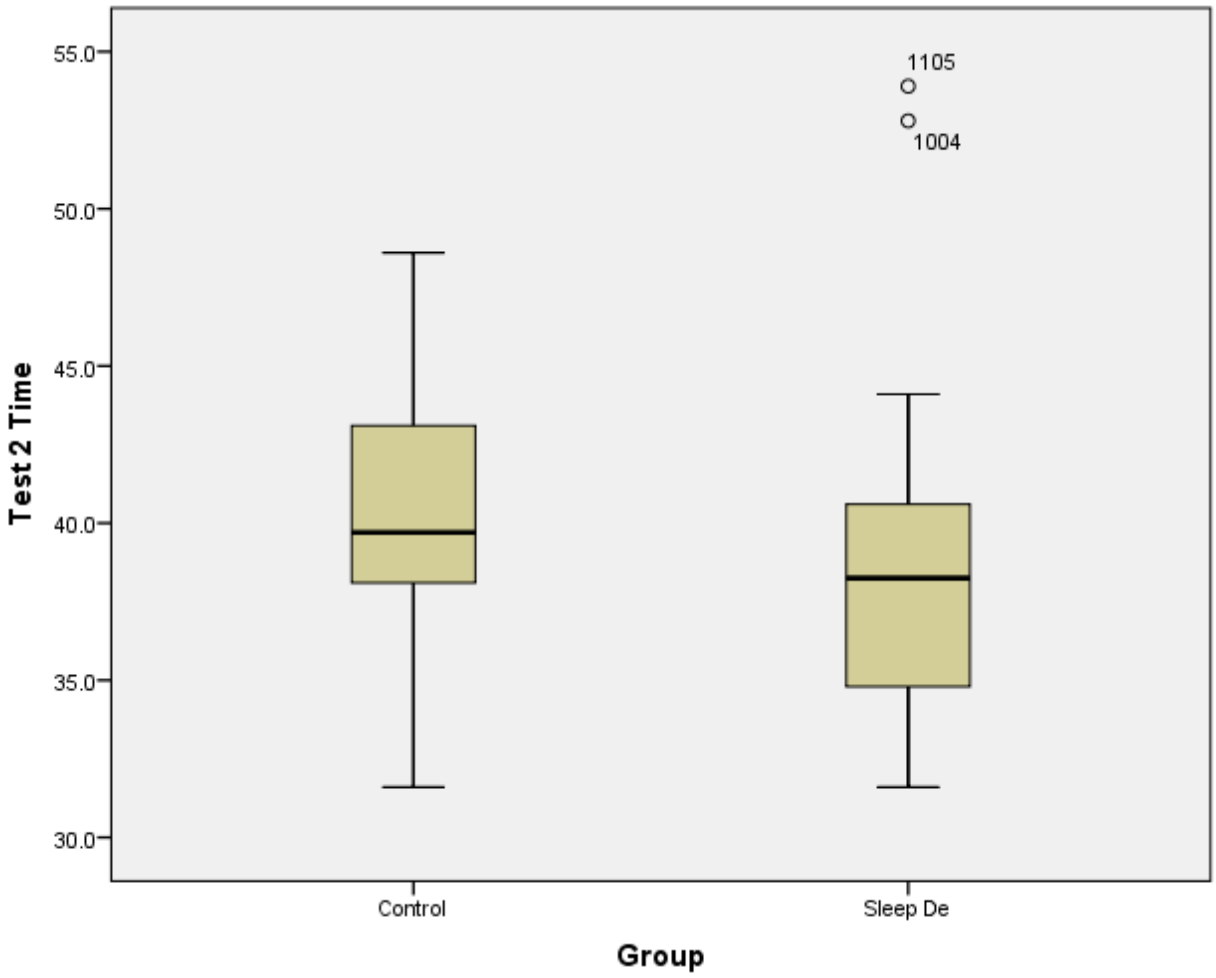



Normal Q-Q Plot of Test 2 Time
for Group= Sleep Deprivation
Expected Normal
3
2
1
0
-1
-2
30
35
40
45
50
55
60
Observed Value

Detrended Normal Q-Q Plots

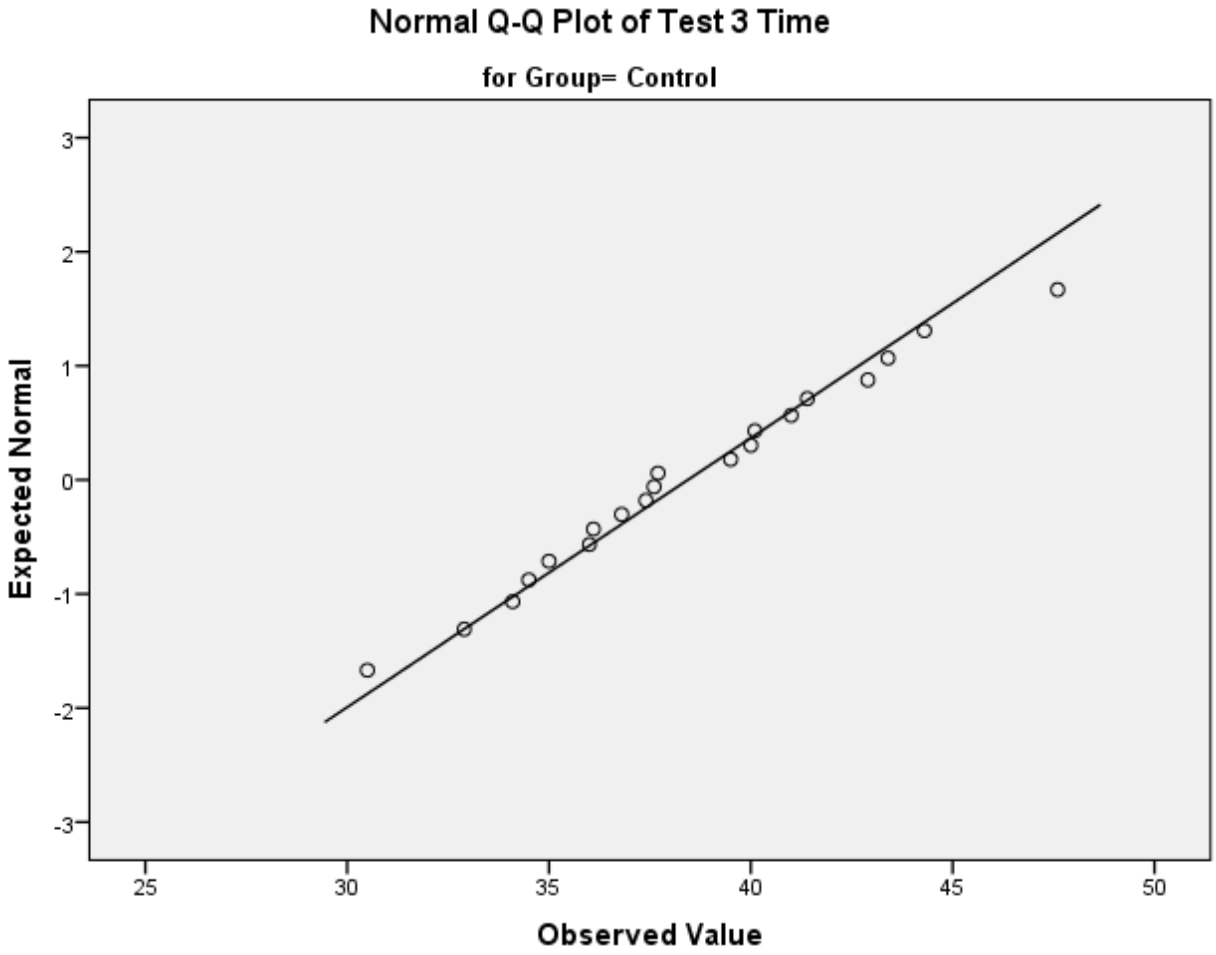


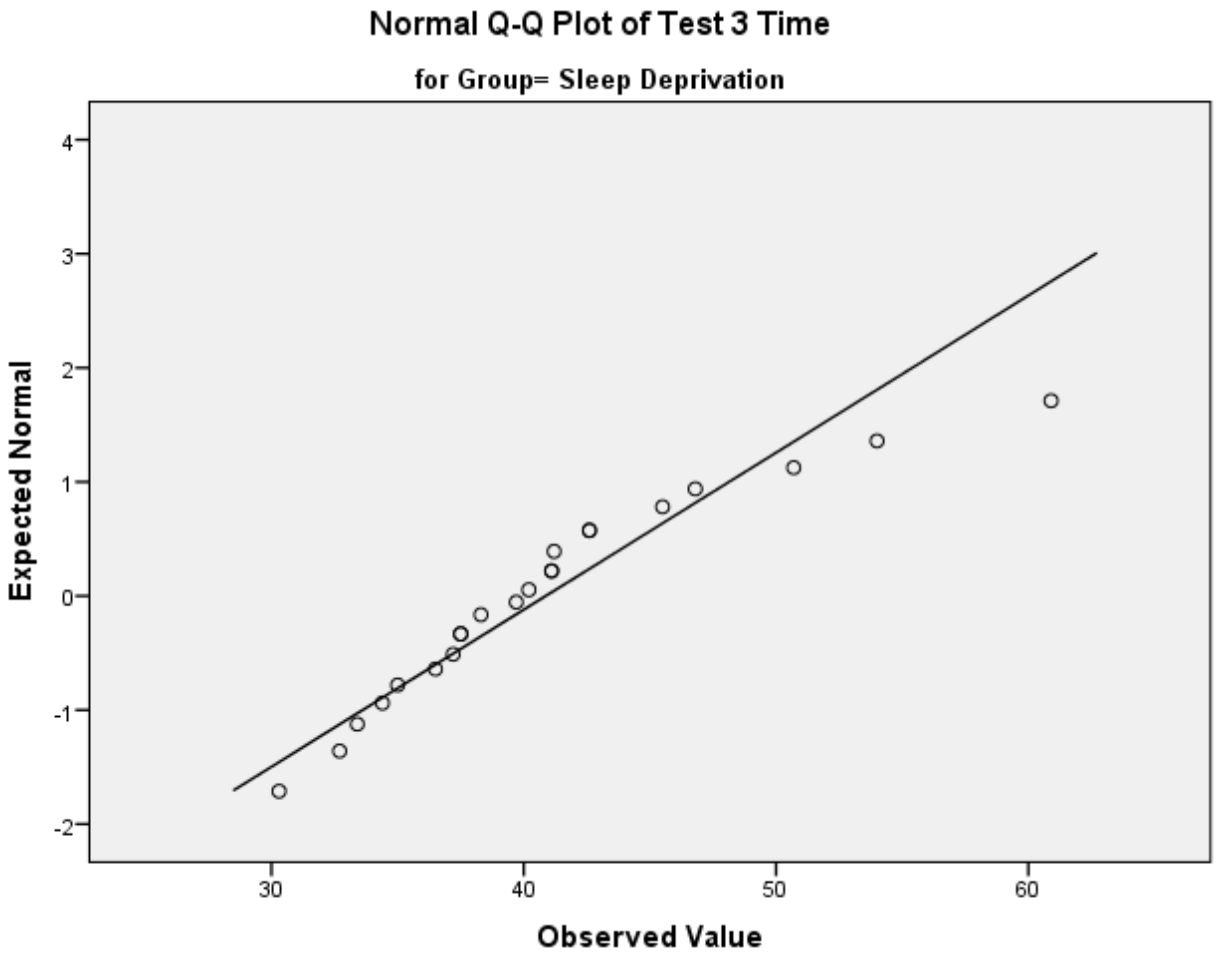

Detrended Normal Q-Q Plot of Test 2 Time
for Group= Sleep Deprivation
Dev from Normal
1.5
1.0
0.5
0.0
-0.5
30
35
40
45
50
55
Observed Value


55.0
50.0
45.0
40.0
35.0
30.0
Test 2 Time
1105
1004
Control
Sleep De
Group

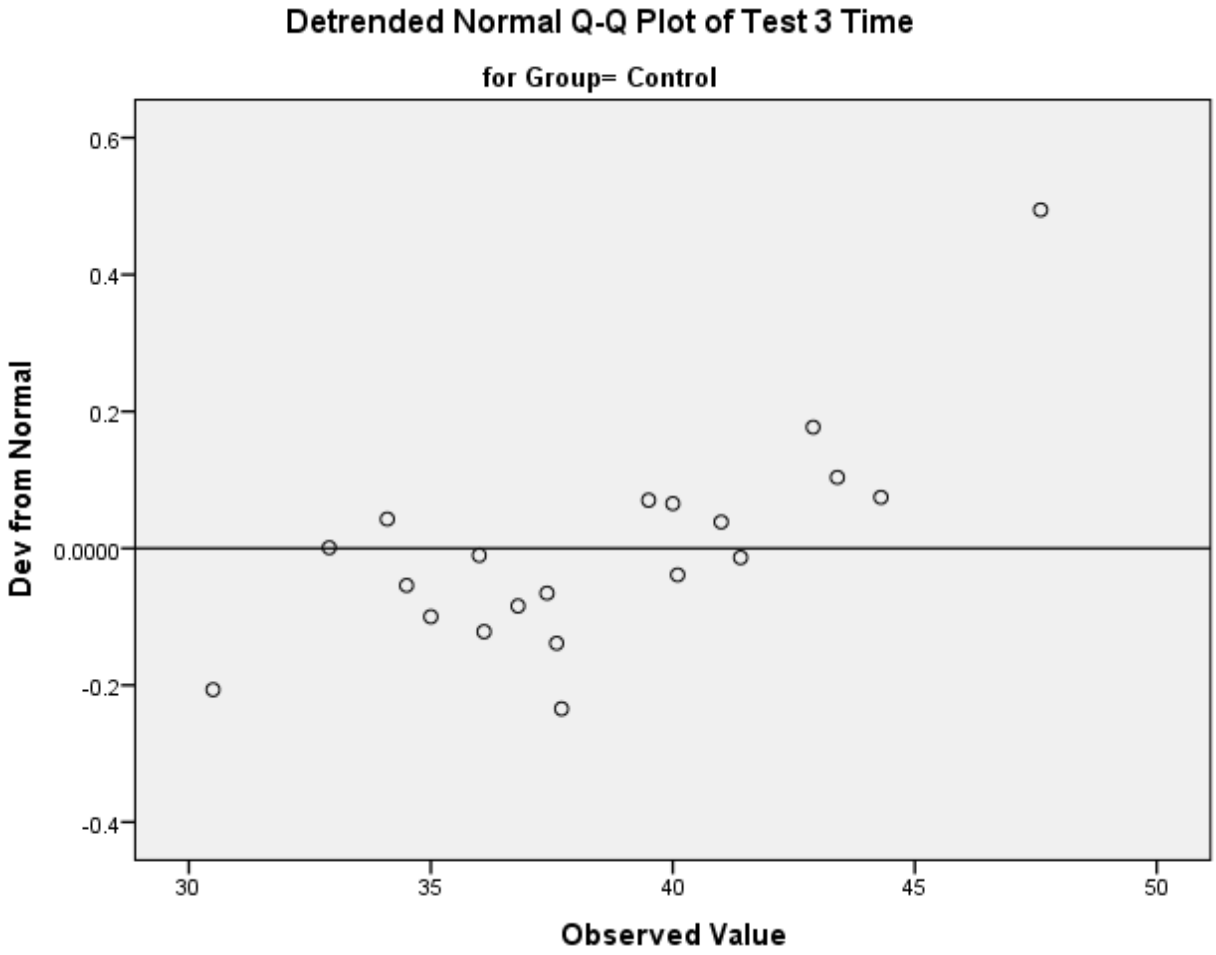
Test 3 Time

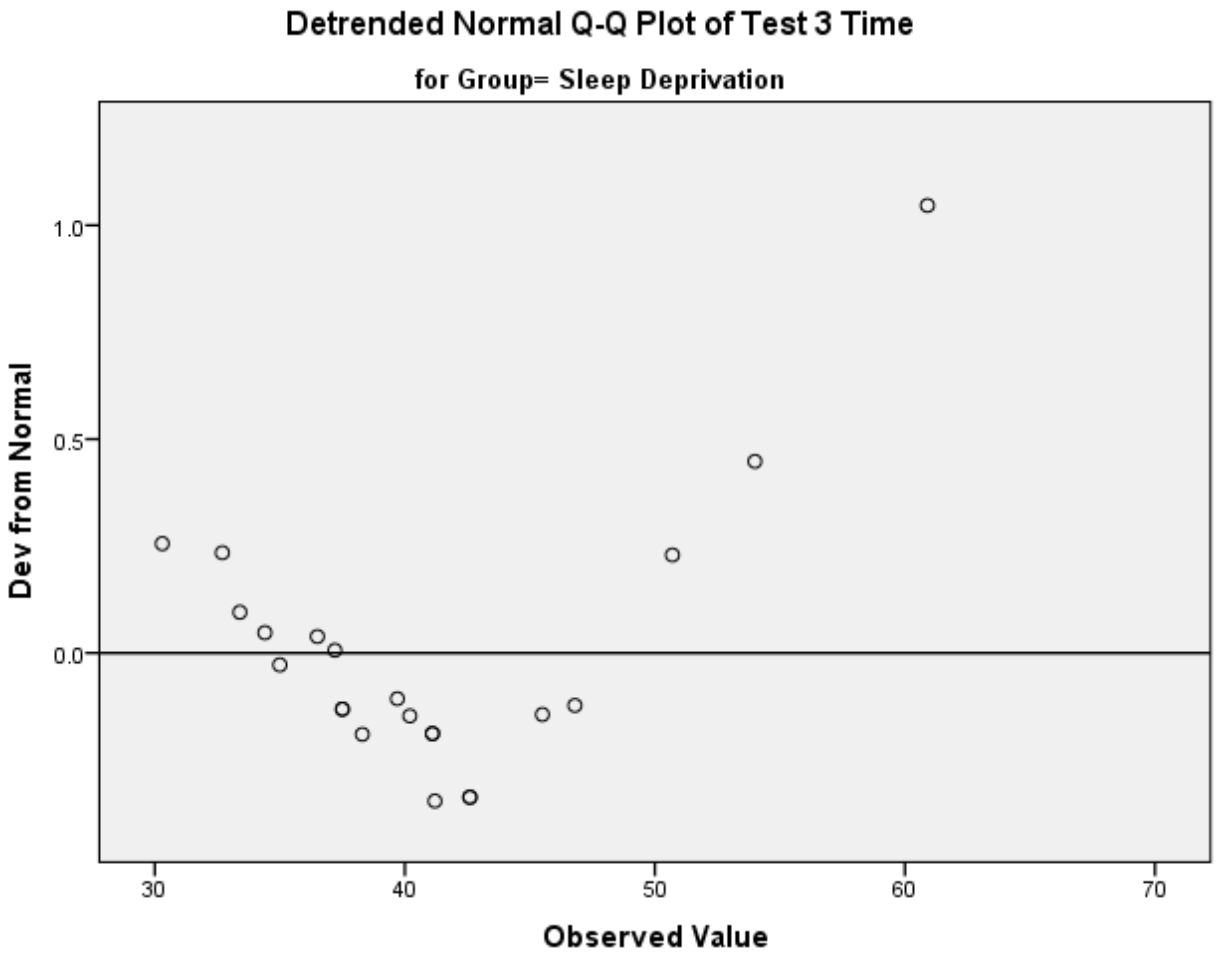
Normal Q-Q Plots

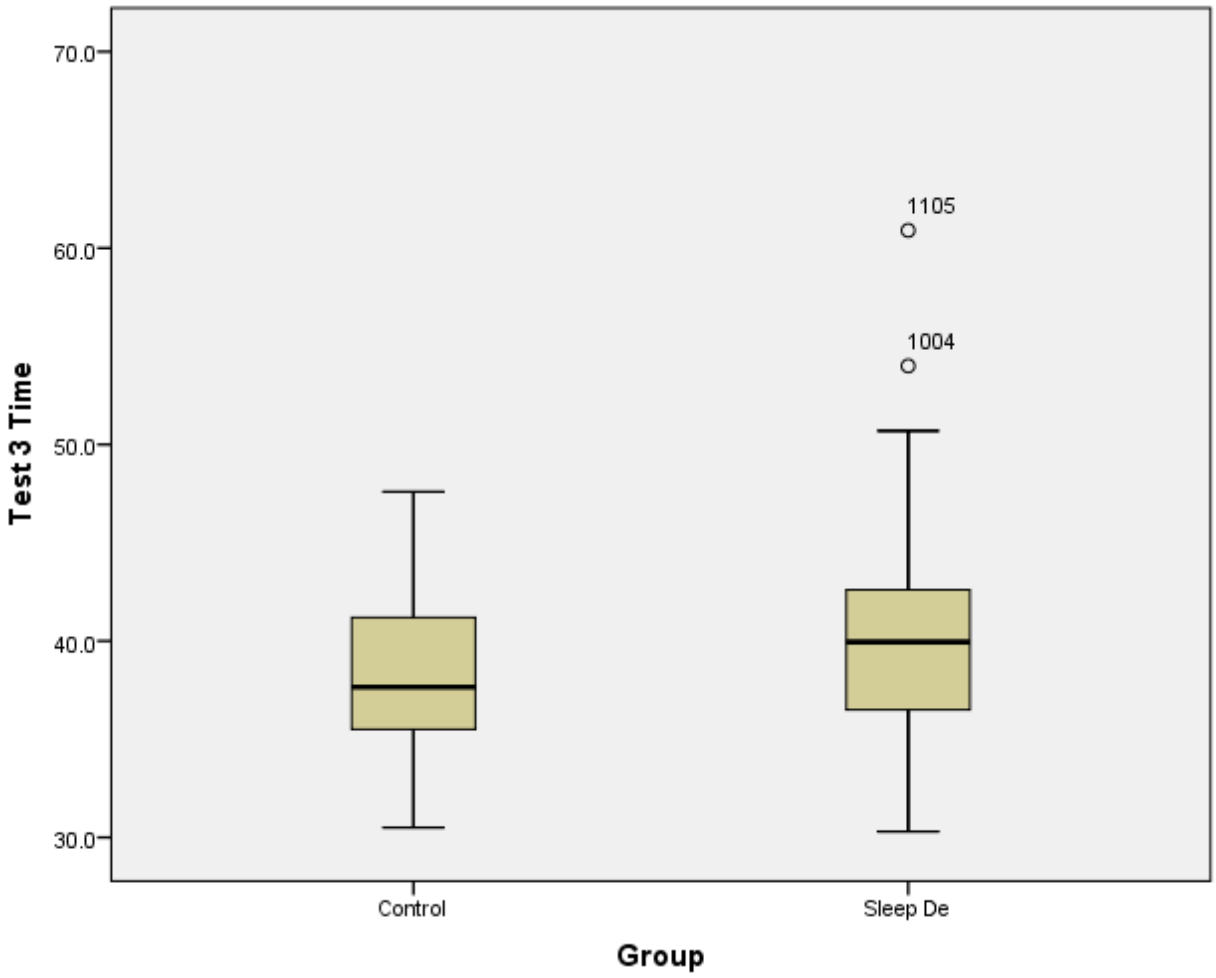



Normal Q-Q Plot of Test 3 Time
for Group= Sleep Deprivation
Expected Normal
Observed Value
4
3
2
1
0
-1
-2
30
40
50
60

Detrended Normal Q-Q Plots




Detrended Normal Q-Q Plot of Test 3 Time
for Group= Sleep Deprivation
Dev from Normal
1.0
0.5
0.0
30
40
50
60
70
Observed Value




```
GLM Test1time Test2Time Test3Time BY Group
  /WSFACTOR=Time 3 Polynomial
  /METHOD=SSTYPE(3)
  /PLOT=PROFILE(Time*Group)
  /EMMEANS=TABLES(OVERALL)
  /EMMEANS=TABLES(Group) COMPARE ADJ(BONFERRONI)
  /EMMEANS=TABLES(Time) COMPARE ADJ(BONFERRONI)
  /EMMEANS=TABLES(Group*Time) compare(group) adj (bonferroni)
 /EMMEANS=TABLES(Group*Time) compare(time) adj (bonferroni)
  /PRINT=DESCRIPTIVE ETASQ OPOWER HOMOGENEITY
  /CRITERIA=ALPHA(.05)
  /WSDESIGN=Time
  /DESIGN=Group.
```

General Linear Model

Notes

Output Created		26-FEB-2018 19:19:26
Comments		
Input	Active Dataset	DataSet1
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	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	42
Missing Value Handling	Definition of Missing	User-defined missing values are treated as missing.
	Cases Used	Statistics are based on all cases with valid data for all variables in the model.

Syntax		GLM Test1time Test2Time Test3Time BY Group /WSFACTOR=Time 3 Polynomial /METHOD=SSTYPE(3) /PLOT=PROFILE(Time*Group) /EMMEANS=TABLES(OVERALL) /EMMEANS=TABLES(Group) COMPARE ADJ(BONFERRONI) /EMMEANS=TABLES(Time) COMPARE ADJ(BONFERRONI) /EMMEANS=TABLES(Group*Time) compare(group) adj (bonferroni) /EMMEANS=TABLES(Group*Time) compare(time) adj (bonferroni) /PRINT=DESCRIPTIVE ETASQ OPOWER HOMOGENEITY /CRITERIA=ALPHA(.05) /WSDESIGN=Time /DESIGN=Group.
Resources	Processor Time	00:00:00.31
	Elapsed Time	00:00:00.19

Within-Subjects Factors

Measure: MEASURE_1

Time	Dependent Variable
1	Test1time
2	Test2Time
3	Test3Time

Between-Subjects Factors

		Value Label	N
Group	0	Control	20
	1	Sleep Deprivation	22

Descriptive Statistics

	Group	Mean	Std. Deviation	N
Test 1 time	Control	42.045	4.4020	20
	Sleep Deprivation	41.318	5.8049	22
	Total	41.664	5.1356	42
Test 2 Time	Control	40.155	4.1708	20
	Sleep Deprivation	38.695	5.9652	22
	Total	39.390	5.1799	42
Test 3 Time	Control	38.440	4.2349	20
	Sleep Deprivation	40.873	7.2615	22
	Total	39.714	6.0689	42

Box's Test of Equality of Covariance Matrices[a]

Box's M	7.367
F	1.127
df1	6
df2	11288.735
Sig.	.343

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.[a]

a. Design: Intercept + Group
Within Subjects Design: Time

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df	Sig.
Time	Pillai's Trace	.400	12.992[b]	2.000	39.000	.000
	Wilks' Lambda	.600	12.992[b]	2.000	39.000	.000
	Hotelling's Trace	.666	12.992[b]	2.000	39.000	.000
	Roy's Largest Root	.666	12.992[b]	2.000	39.000	.000
Time * Group	Pillai's Trace	.336	9.860[b]	2.000	39.000	.000
	Wilks' Lambda	.664	9.860[b]	2.000	39.000	.000
	Hotelling's Trace	.506	9.860[b]	2.000	39.000	.000
	Roy's Largest Root	.506	9.860[b]	2.000	39.000	.000

Multivariate Tests[a]

Effect		Partial Eta Squared	Noncent. Parameter	Observed Power[c]
Time	Pillai's Trace	.400	25.983	.995
	Wilks' Lambda	.400	25.983	.995
	Hotelling's Trace	.400	25.983	.995
	Roy's Largest Root	.400	25.983	.995
Time * Group	Pillai's Trace	.336	19.720	.976
	Wilks' Lambda	.336	19.720	.976
	Hotelling's Trace	.336	19.720	.976
	Roy's Largest Root	.336	19.720	.976

a. Design: Intercept + Group
Within Subjects Design: Time
b. Exact statistic
c. Computed using alpha = .05

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b] Greenhouse-Geisser
Time	.816	7.944	2	.019	.844

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Epsilon	
	Huynh-Feldt	Lower-bound
Time	.900	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.[a]
a. Design: Intercept + Group
Within Subjects Design: Time
b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
Time	Sphericity Assumed	129.153	2	64.576	12.736	.000
	Greenhouse-Geisser	129.153	1.689	76.476	12.736	.000
	Huynh-Feldt	129.153	1.799	71.784	12.736	.000
	Lower-bound	129.153	1.000	129.153	12.736	.001
Time * Group	Sphericity Assumed	89.639	2	44.820	8.840	.000
	Greenhouse-Geisser	89.639	1.689	53.079	8.840	.001
	Huynh-Feldt	89.639	1.799	49.822	8.840	.001
	Lower-bound	89.639	1.000	89.639	8.840	.005
Error(Time)	Sphericity Assumed	405.628	80	5.070		
	Greenhouse-Geisser	405.628	67.552	6.005		
	Huynh-Feldt	405.628	71.968	5.636		
	Lower-bound	405.628	40.000	10.141		

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Partial Eta Squared	Noncent. Parameter	Observed Power[a]
Time	Sphericity Assumed	.242	25.472	.996
	Greenhouse-Geisser	.242	21.509	.990
	Huynh-Feldt	.242	22.915	.993
	Lower-bound	.242	12.736	.936
Time * Group	Sphericity Assumed	.181	17.679	.967
	Greenhouse-Geisser	.181	14.928	.944
	Huynh-Feldt	.181	15.904	.953
	Lower-bound	.181	8.840	.827
Error(Time)	Sphericity Assumed			
	Greenhouse-Geisser			
	Huynh-Feldt			
	Lower-bound			

a. Computed using alpha = .05

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Time	Type III Sum of Squares	df	Mean Square	F	Sig.
Time	Linear	85.937	1	85.937	11.859	.001
	Quadratic	43.215	1	43.215	14.933	.000
Time * Group	Linear	52.290	1	52.290	7.216	.010
	Quadratic	37.349	1	37.349	12.906	.001
Error(Time)	Linear	289.872	40	7.247		
	Quadratic	115.756	40	2.894		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Time	Partial Eta Squared	Noncent. Parameter	Observed Power[a]
Time	Linear	.229	11.859	.919
	Quadratic	.272	14.933	.965
Time * Group	Linear	.153	7.216	.746
	Quadratic	.244	12.906	.939
Error(Time)	Linear			
	Quadratic			

a. Computed using alpha = .05

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
Test 1 time	.531	1	40	.470
Test 2 Time	1.292	1	40	.262
Test 3 Time	2.308	1	40	.137

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.[a]

a. Design: Intercept + Group
Within Subjects Design: Time

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	203709.469	1	203709.469	2549.552	.000	.985
Group	.212	1	.212	.003	.959	.000
Error	3196.005	40	79.900			

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Noncent. Parameter	Observed Power[a]
Intercept	2549.552	1.000
Group	.003	.050
Error		

a. Computed using alpha = .05

Estimated Marginal Means

1. Grand Mean

Measure: MEASURE_1

Mean	Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
40.254	.797	38.643	41.866

2. Group

Estimates

Measure: MEASURE_1

Group	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Control	40.213	1.154	37.881	42.546
Sleep Deprivation	40.295	1.100	38.072	42.519

Pairwise Comparisons

Measure: MEASURE_1

(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.[a]	95% Confidence Interval for Difference[a] Lower Bound
Control	Sleep Deprivation	-.082	1.594	.959	-3.305
Sleep Deprivation	Control	.082	1.594	.959	-3.140

Pairwise Comparisons

Measure: MEASURE_1

(I) Group	(J) Group	95% Confidence Interval for Difference Upper Bound
Control	Sleep Deprivation	3.140
Sleep Deprivation	Control	3.305

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

Univariate Tests

Measure: MEASURE_1

	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.071	1	.071	.003	.959	.000
Error	1065.335	40	26.633			

Univariate Tests

Measure: MEASURE_1

	Noncent. Parameter	Observed Power[a]
Contrast	.003	.050
Error		

The F tests the effect of Group. This test is based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Computed using alpha = .05

2. Time

Estimates

Measure: MEASURE_1

Time	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	41.682	.801	40.062	43.301
2	39.425	.802	37.805	41.046
3	39.656	.929	37.778	41.535

Pairwise Comparisons

Measure: MEASURE_1

(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
1	2	2.256*	.437	.000	1.164	3.349
	3	2.025*	.588	.004	.556	3.495
2	1	-2.256*	.437	.000	-3.349	-1.164
	3	-.231	.435	1.000	-1.318	.855
3	1	-2.025*	.588	.004	-3.495	-.556
	2	.231	.435	1.000	-.855	1.318

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Multivariate Tests

	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Pillai's trace	.400	12.992[a]	2.000	39.000	.000	.400
Wilks' lambda	.600	12.992[a]	2.000	39.000	.000	.400
Hotelling's trace	.666	12.992[a]	2.000	39.000	.000	.400
Roy's largest root	.666	12.992[a]	2.000	39.000	.000	.400

Multivariate Tests

	Noncent. Parameter	Observed Power[b]
Pillai's trace	25.983	.995
Wilks' lambda	25.983	.995
Hotelling's trace	25.983	.995
Roy's largest root	25.983	.995

Each F tests the multivariate effect of Time. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Exact statistic

b. Computed using alpha = .05

4. Group * Time

Estimates

Measure: MEASURE_1

				95% Confidence Interval	
Group	Time	Mean	Std. Error	Lower Bound	Upper Bound
Control	1	42.045	1.160	39.701	44.389
	2	40.155	1.161	37.809	42.501
	3	38.440	1.345	35.721	41.159
Sleep Deprivation	1	41.318	1.106	39.084	43.553
	2	38.695	1.107	36.459	40.932
	3	40.873	1.283	38.280	43.465

Pairwise Comparisons

Measure: MEASURE_1

						95% Confidence Interval for Difference[a]
Time	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.[a]	Lower Bound
1	Control	Sleep Deprivation	.727	1.602	.653	-2.511
	Sleep Deprivation	Control	-.727	1.602	.653	-3.965
2	Control	Sleep Deprivation	1.460	1.604	.368	-1.782
	Sleep Deprivation	Control	-1.460	1.604	.368	-4.701
3	Control	Sleep Deprivation	-2.433	1.859	.198	-6.190
	Sleep Deprivation	Control	2.433	1.859	.198	-1.324

Pairwise Comparisons

Measure: MEASURE_1

Time	(I) Group	(J) Group	95% Confidence Interval for Difference Upper Bound
1	Control	Sleep Deprivation	3.965
	Sleep Deprivation	Control	2.511
2	Control	Sleep Deprivation	4.701
	Sleep Deprivation	Control	1.782
3	Control	Sleep Deprivation	1.324
	Sleep Deprivation	Control	6.190

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

Univariate Tests

Measure: MEASURE_1

Time		Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
1	Contrast	5.534	1	5.534	.206	.653	.005
	Error	1075.802	40	26.895			
2	Contrast	22.317	1	22.317	.828	.368	.020
	Error	1077.759	40	26.944			
3	Contrast	62.000	1	62.000	1.713	.198	.041
	Error	1448.072	40	36.202			

Univariate Tests

Measure: MEASURE_1

Time		Noncent. Parameter	Observed Power[a]
1	Contrast	.206	.073
	Error		
2	Contrast	.828	.144
	Error		
3	Contrast	1.713	.248
	Error		

Each F tests the simple effects of Group within each level combination of the other effects shown. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Computed using alpha = .05

5. Group * Time

Estimates

Measure: MEASURE_1

Group	Time	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Control	1	42.045	1.160	39.701	44.389
	2	40.155	1.161	37.809	42.501
	3	38.440	1.345	35.721	41.159
Sleep Deprivation	1	41.318	1.106	39.084	43.553
	2	38.695	1.107	36.459	40.932
	3	40.873	1.283	38.280	43.465

Pairwise Comparisons

Measure: MEASURE_1

Group	(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]
						Lower Bound
Control	1	2	1.890*	.633	.014	.309
		3	3.605*	.851	.000	1.478
	2	1	-1.890*	.633	.014	-3.471
		3	1.715*	.629	.028	.142
	3	1	-3.605*	.851	.000	-5.732
		2	-1.715*	.629	.028	-3.288
Sleep Deprivation	1	2	2.623*	.603	.000	1.115
		3	.445	.812	1.000	-1.583
	2	1	-2.623*	.603	.000	-4.130
		3	-2.177*	.600	.002	-3.677
	3	1	-.445	.812	1.000	-2.474
		2	2.177*	.600	.002	.678

Pairwise Comparisons

Measure: MEASURE_1

Group	(I) Time	(J) Time	95% Confidence Interval for Difference Upper Bound
Control	1	2	3.471
		3	5.732
	2	1	-.309
		3	3.288
	3	1	-1.478
		2	-.142
Sleep Deprivation	1	2	4.130
		3	2.474
	2	1	-1.115
		3	-.678
	3	1	1.583
		2	3.677

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Multivariate Tests

Group		Value	F	Hypothesis df	Error df	Sig.
Control	Pillai's trace	.310	8.756[a]	2.000	39.000	.001
	Wilks' lambda	.690	8.756[a]	2.000	39.000	.001
	Hotelling's trace	.449	8.756[a]	2.000	39.000	.001
	Roy's largest root	.449	8.756[a]	2.000	39.000	.001
Sleep Deprivation	Pillai's trace	.424	14.363[a]	2.000	39.000	.000
	Wilks' lambda	.576	14.363[a]	2.000	39.000	.000
	Hotelling's trace	.737	14.363[a]	2.000	39.000	.000
	Roy's largest root	.737	14.363[a]	2.000	39.000	.000

Multivariate Tests

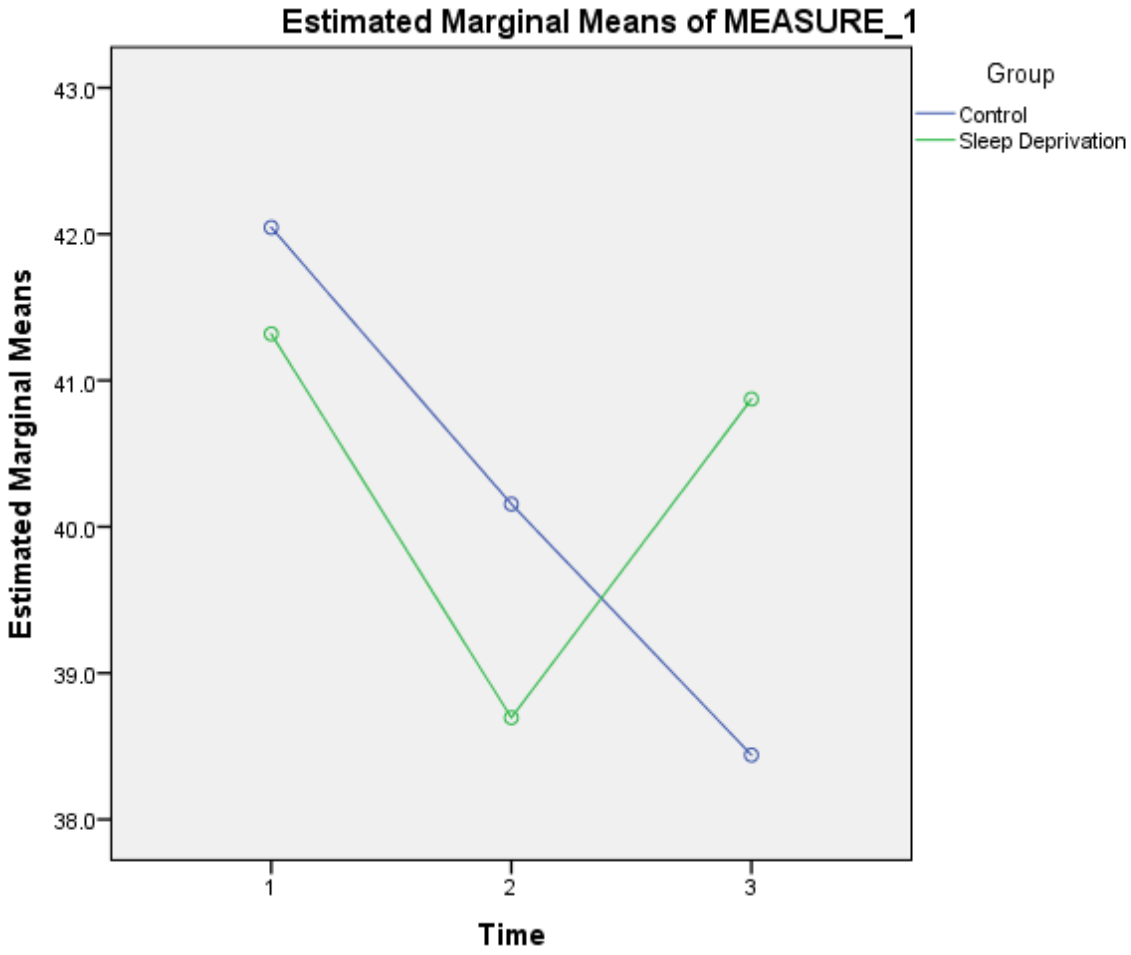
Group		Partial Eta Squared	Noncent. Parameter	Observed Power[b]
Control	Pillai's trace	.310	17.512	.959
	Wilks' lambda	.310	17.512	.959
	Hotelling's trace	.310	17.512	.959
	Roy's largest root	.310	17.512	.959
Sleep Deprivation	Pillai's trace	.424	28.726	.998
	Wilks' lambda	.424	28.726	.998
	Hotelling's trace	.424	28.726	.998
	Roy's largest root	.424	28.726	.998

Each F tests the multivariate simple effects of Time within each level combination of the other effects shown. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Exact statistic

b. Computed using alpha = .05

Profile Plots

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Explore

Notes

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	Cases Used	Statistics are based on cases with no missing values for any dependent variable or factor used.
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Sleep Dep 1=yes 0=no

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	Sleep Dep 1=yes 0=no	N	Percent	N	Percent	N	Percent
Errors 1	Control	20	100.0%	0	0.0%	20	100.0%
	Sleep Deprivration	22	100.0%	0	0.0%	22	100.0%
Errors 2	Control	20	100.0%	0	0.0%	20	100.0%
	Sleep Deprivration	22	100.0%	0	0.0%	22	100.0%
Errors 3	Control	20	100.0%	0	0.0%	20	100.0%
	Sleep Deprivration	22	100.0%	0	0.0%	22	100.0%

Descriptives

	Sleep Dep 1=yes 0=no			Statistic	Std. Error
Errors 1	Control	Mean		.50	.170
		95% Confidence Interval for Mean	Lower Bound	.14	
			Upper Bound	.86	
		5% Trimmed Mean		.44	
		Median		.00	
		Variance		.579	
		Std. Deviation		.761	
		Minimum		0	
		Maximum		2	
		Range		2	
		Interquartile Range		1	
		Skewness		1.195	.512
		Kurtosis		-.037	.992
	Sleep Deprivration	Mean		.18	.142
		95% Confidence Interval for Mean	Lower Bound	-.11	
			Upper Bound	.48	
		5% Trimmed Mean		.05	
		Median		.00	
		Variance		.442	
		Std. Deviation		.664	
		Minimum		0	
		Maximum		3	
		Range		3	

		Interquartile Range		0	
		Skewness		4.072	.491
		Kurtosis		17.185	.953
Errors 2	Control	Mean		.50	.246
		95% Confidence Interval for Mean	Lower Bound	-.01	
			Upper Bound	1.01	
		5% Trimmed Mean		.33	
		Median		.00	
		Variance		1.211	
		Std. Deviation		1.100	
		Minimum		0	
		Maximum		4	
		Range		4	
		Interquartile Range		1	
		Skewness		2.503	.512
		Kurtosis		5.840	.992
	Sleep Deprivration	Mean		.45	.183
		95% Confidence Interval for Mean	Lower Bound	.07	
			Upper Bound	.83	
		5% Trimmed Mean		.34	
		Median		.00	
		Variance		.736	
		Std. Deviation		.858	
		Minimum		0	
		Maximum		3	
		Range		3	
		Interquartile Range		1	
		Skewness		1.897	.491
		Kurtosis		2.880	.953
Errors 3	Control	Mean		.25	.099
		95% Confidence Interval for Mean	Lower Bound	.04	
			Upper Bound	.46	
		5% Trimmed Mean		.22	
		Median		.00	
		Variance		.197	
		Std. Deviation		.444	
		Minimum		0	
		Maximum		1	
		Range		1	

		Interquartile Range		1	
		Skewness		1.251	.512
		Kurtosis		-.497	.992
	Sleep Deprivration	Mean		.55	.215
		95% Confidence Interval for Mean	Lower Bound	.10	
			Upper Bound	.99	
		5% Trimmed Mean		.39	
		Median		.00	
		Variance		1.022	
		Std. Deviation		1.011	
		Minimum		0	
		Maximum		4	
		Range		4	
		Interquartile Range		1	
		Skewness		2.299	.491
		Kurtosis		5.805	.953

Notes

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Syntax		GLM Errors1 Errors2 Errors3 BY SleepDep1yes0no /WSFACTOR=Time 3 Polynomial /METHOD=SSTYPE(3) /POSTHOC=SleepDep1yes0 no(BONFERRONI) /PLOT=PROFILE(Time*Sleep Dep1yes0no) /EMMEANS=TABLES(OVER ALL) /EMMEANS=TABLES(Sleep Dep1yes0no) COMPARE(time) ADJ(BONFERRONI) /EMMEANS=TABLES(Time) COMPARE(SleepDep1yes0n o) ADJ(BONFERRONI) /EMMEANS=TABLES(Sleep Dep1yes0no*Time) /PRINT=DESCRIPTIVE ETASQ OPOWER HOMOGENEITY /CRITERIA=ALPHA(.05) /WSDESIGN=Time /DESIGN=SleepDep1yes0no.
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GLM Errors1 Errors2 Errors3 BY SleepDep1yes0no
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/EMMEANS=TABLES(SleepDep1yes0no) COMPARE ADJ(BONFERRONI)

/EMMEANS=TABLES(Time) COMPARE ADJ(BONFERRONI)
/EMMEANS=TABLES(SleepDep1yes0no*Time) compare(Time) adj (bonferroni)
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General Linear Model

Notes

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Missing Value Handling	Definition of Missing	User-defined missing values are treated as missing.
	Cases Used	Statistics are based on all cases with valid data for all variables in the model.

Syntax		GLM Errors1 Errors2 Errors3 BY SleepDep1yes0no /WSFACTOR=Time 3 Polynomial /METHOD=SSTYPE(3) /POSTHOC=SleepDep1yes0no(BONFERRONI) /PLOT=PROFILE(Time*SleepDep1yes0no) /EMMEANS=TABLES(OVERALL) /EMMEANS=TABLES(SleepDep1yes0no) COMPARE ADJ(BONFERRONI) /EMMEANS=TABLES(Time) COMPARE ADJ(BONFERRONI) /EMMEANS=TABLES(SleepDep1yes0no*Time) compare(Time) adj (bonferroni) /EMMEANS=TABLES(SleepDep1yes0no*Time) compare(SleepDep1yes0no) adj (bonferroni) /PRINT=DESCRIPTIVE ETASQ OPOWER HOMOGENEITY /CRITERIA=ALPHA(.05) /WSDESIGN=Time /DESIGN=SleepDep1yes0no.
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Warnings

Post hoc tests are not performed for Sleep Dep 1=yes 0=no because there are fewer than three groups.

Within-Subjects Factors

Measure: MEASURE_1

Time	Dependent Variable
1	Errors1
2	Errors2
3	Errors3

Between-Subjects Factors

		Value Label	N
Sleep Dep 1=yes 0=no	0	Control	20
	1	Sleep Deprivration	22

Descriptive Statistics

	Sleep Dep 1=yes 0=no	Mean	Std. Deviation	N
Errors 1	Control	.50	.761	20
	Sleep Deprivration	.18	.664	22
	Total	.33	.721	42
Errors 2	Control	.50	1.100	20
	Sleep Deprivration	.45	.858	22
	Total	.48	.969	42
Errors 3	Control	.25	.444	20
	Sleep Deprivration	.55	1.011	22
	Total	.40	.798	42

Box's Test of Equality of Covariance Matrices[a]

Box's M	28.181
F	4.311
df1	6
df2	11288.735
Sig.	.000

Tests the null hypothesis that the observed covariance matrices of the dependent variables are equal across groups.[a]

a. Design: Intercept + SleepDep1yes0no
Within Subjects Design: Time

Multivariate Tests[a]

Effect		Value	F	Hypothesis df	Error df
Time	Pillai's Trace	.021	.419[b]	2.000	39.000
	Wilks' Lambda	.979	.419[b]	2.000	39.000
	Hotelling's Trace	.021	.419[b]	2.000	39.000
	Roy's Largest Root	.021	.419[b]	2.000	39.000
Time * SleepDep1yes0no	Pillai's Trace	.210	5.184[b]	2.000	39.000
	Wilks' Lambda	.790	5.184[b]	2.000	39.000
	Hotelling's Trace	.266	5.184[b]	2.000	39.000
	Roy's Largest Root	.266	5.184[b]	2.000	39.000

Multivariate Tests[a]

Effect		Sig.	Partial Eta Squared	Noncent. Parameter
Time	Pillai's Trace	.661	.021	.837
	Wilks' Lambda	.661	.021	.837
	Hotelling's Trace	.661	.021	.837
	Roy's Largest Root	.661	.021	.837
Time * SleepDep1yes0no	Pillai's Trace	.010	.210	10.367
	Wilks' Lambda	.010	.210	10.367
	Hotelling's Trace	.010	.210	10.367
	Roy's Largest Root	.010	.210	10.367

Multivariate Tests[a]

Effect		Observed Power[c]
Time	Pillai's Trace	.113
	Wilks' Lambda	.113
	Hotelling's Trace	.113
	Roy's Largest Root	.113
Time * SleepDep1yes0no	Pillai's Trace	.798
	Wilks' Lambda	.798
	Hotelling's Trace	.798
	Roy's Largest Root	.798

a. Design: Intercept + SleepDep1yes0no

Within Subjects Design: Time

b. Exact statistic

c. Computed using alpha = .05

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[b] Greenhouse-Geisser
Time	.669	15.682	2	.000	.751

Mauchly's Test of Sphericity[a]

Measure: MEASURE_1

Within Subjects Effect	Epsilon	
	Huynh-Feldt	Lower-bound
Time	.794	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.[a]

a. Design: Intercept + SleepDep1yes0no

Within Subjects Design: Time

b. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F
Time	Sphericity Assumed	.393	2	.197	.450
	Greenhouse-Geisser	.393	1.503	.262	.450
	Huynh-Feldt	.393	1.587	.248	.450
	Lower-bound	.393	1.000	.393	.450
Time * SleepDep1yes0no	Sphericity Assumed	1.981	2	.990	2.268
	Greenhouse-Geisser	1.981	1.503	1.318	2.268
	Huynh-Feldt	1.981	1.587	1.248	2.268
	Lower-bound	1.981	1.000	1.981	2.268
Error(Time)	Sphericity Assumed	34.924	80	.437	
	Greenhouse-Geisser	34.924	60.101	.581	
	Huynh-Feldt	34.924	63.491	.550	
	Lower-bound	34.924	40.000	.873	

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Sig.	Partial Eta Squared	Noncent. Parameter
Time	Sphericity Assumed	.639	.011	.901
	Greenhouse-Geisser	.584	.011	.677
	Huynh-Feldt	.594	.011	.715
	Lower-bound	.506	.011	.450
Time * SleepDep1yes0no	Sphericity Assumed	.110	.054	4.537
	Greenhouse-Geisser	.125	.054	3.408
	Huynh-Feldt	.123	.054	3.601
	Lower-bound	.140	.054	2.268
Error(Time)	Sphericity Assumed			
	Greenhouse-Geisser			
	Huynh-Feldt			
	Lower-bound			

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Observed Power[a]
Time	Sphericity Assumed	.121
	Greenhouse-Geisser	.111
	Huynh-Feldt	.113
	Lower-bound	.100
Time * SleepDep1yes0no	Sphericity Assumed	.449
	Greenhouse-Geisser	.384
	Huynh-Feldt	.396
	Lower-bound	.312
Error(Time)	Sphericity Assumed	
	Greenhouse-Geisser	
	Huynh-Feldt	
	Lower-bound	

a. Computed using alpha = .05

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Time	Type III Sum of Squares	df	Mean Square	F
Time	Linear	.068	1	.068	.365
	Quadratic	.326	1	.326	.474
Time * SleepDep1yes0no	Linear	1.972	1	1.972	10.632
	Quadratic	.008	1	.008	.012
Error(Time)	Linear	7.420	40	.186	
	Quadratic	27.504	40	.688	

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	Time	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power[a]
Time	Linear	.549	.009	.365	.091
	Quadratic	.495	.012	.474	.103
Time * SleepDep1yes0no	Linear	.002	.210	10.632	.889
	Quadratic	.914	.000	.012	.051
Error(Time)	Linear				
	Quadratic				

a. Computed using alpha = .05

Levene's Test of Equality of Error Variances[a]

	F	df1	df2	Sig.
Errors 1	4.540	1	40	.039
Errors 2	.188	1	40	.667
Errors 3	5.577	1	40	.023

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.[a]

a. Design: Intercept + SleepDep1yes0no

Within Subjects Design: Time

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	20.651	1	20.651	16.855	.000	.296
SleepDep1yes0no	.016	1	.016	.013	.909	.000
Error	49.008	40	1.225			

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Noncent. Parameter	Observed Power[a]
Intercept	16.855	.980
SleepDep1yes0no	.013	.051
Error		

a. Computed using alpha = .05

Estimated Marginal Means

1. Grand Mean

Measure: MEASURE_1

Mean	Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
.405	.099	.206	.605

2. Sleep Dep 1=yes 0=no

Estimates

Measure: MEASURE_1

Sleep Dep 1=yes 0=no	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Control	.417	.143	.128	.705
Sleep Deprivration	.394	.136	.119	.669

Pairwise Comparisons

Measure: MEASURE_1

(I) Sleep Dep 1=yes 0=no	(J) Sleep Dep 1=yes 0=no	Mean Difference (I-J)	Std. Error	Sig.[a]
Control	Sleep Deprivration	.023	.197	.909
Sleep Deprivration	Control	-.023	.197	.909

Pairwise Comparisons

Measure: MEASURE_1

		95% Confidence Interval for Difference[a]	
(I) Sleep Dep 1=yes 0=no	(J) Sleep Dep 1=yes 0=no	Lower Bound	Upper Bound
Control	Sleep Deprivration	-.376	.422
Sleep Deprivration	Control	-.422	.376

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

Univariate Tests

Measure: MEASURE_1

	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.005	1	.005	.013	.909	.000
Error	16.336	40	.408			

Univariate Tests

Measure: MEASURE_1

	Noncent. Parameter	Observed Power[a]
Contrast	.013	.051
Error		

The F tests the effect of Sleep Dep 1=yes 0=no. This test is based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Computed using alpha = .05

3. Time

Estimates

Measure: MEASURE_1

Time	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	.341	.110	.119	.563
2	.477	.151	.171	.783
3	.398	.123	.150	.646

Pairwise Comparisons

Measure: MEASURE_1

(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.[a]	95% Confidence Interval for Difference[a]	
					Lower Bound	Upper Bound
1	2	-.136	.163	1.000	-.543	.270
	3	-.057	.094	1.000	-.292	.178
2	1	.136	.163	1.000	-.270	.543
	3	.080	.165	1.000	-.332	.492
3	1	.057	.094	1.000	-.178	.292
	2	-.080	.165	1.000	-.492	.332

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

Multivariate Tests

	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Pillai's trace	.021	.419[a]	2.000	39.000	.661	.021
Wilks' lambda	.979	.419[a]	2.000	39.000	.661	.021
Hotelling's trace	.021	.419[a]	2.000	39.000	.661	.021
Roy's largest root	.021	.419[a]	2.000	39.000	.661	.021

Multivariate Tests

	Noncent. Parameter	Observed Power[b]
Pillai's trace	.837	.113
Wilks' lambda	.837	.113
Hotelling's trace	.837	.113
Roy's largest root	.837	.113

Each F tests the multivariate effect of Time. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Exact statistic

b. Computed using alpha = .05

4. Sleep Dep 1=yes 0=no * Time

Estimates

Measure: MEASURE_1

				95% Confidence Interval	
Sleep Dep 1=yes 0=no	Time	Mean	Std. Error	Lower Bound	Upper Bound
Control	1	.500	.159	.178	.822
	2	.500	.219	.057	.943
	3	.250	.177	-.109	.609
Sleep Deprivration	1	.182	.152	-.125	.489
	2	.455	.209	.032	.877
	3	.545	.169	.203	.887

Pairwise Comparisons

Measure: MEASURE_1

Sleep Dep 1=yes 0=no	(I) Time	(J) Time	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b] Lower Bound
Control	1	2	.000	.235	1.000	-.588
		3	.250	.136	.222	-.090
	2	1	.000	.235	1.000	-.588
		3	.250	.239	.903	-.346
	3	1	-.250	.136	.222	-.590
		2	-.250	.239	.903	-.846
Sleep Deprivation	1	2	-.273	.225	.695	-.834
		3	-.364*	.130	.023	-.688
	2	1	.273	.225	.695	-.288
		3	-.091	.228	1.000	-.660
	3	1	.364*	.130	.023	.039
		2	.091	.228	1.000	-.478

Pairwise Comparisons

Measure: MEASURE_1

Sleep Dep 1=yes 0=no	(I) Time	(J) Time	95% Confidence Interval for Difference Upper Bound
Control	1	2	.588
		3	.590
	2	1	.588
		3	.846
	3	1	.090
		2	.346
Sleep Deprivation	1	2	.288
		3	-.039
	2	1	.834
		3	.478
	3	1	.688
		2	.660

Based on estimated marginal means

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Multivariate Tests

Sleep Dep 1=yes 0=no		Value	F	Hypothesis df	Error df	Sig.
Control	Pillai's trace	.083	1.767[a]	2.000	39.000	.184
	Wilks' lambda	.917	1.767[a]	2.000	39.000	.184
	Hotelling's trace	.091	1.767[a]	2.000	39.000	.184
	Roy's largest root	.091	1.767[a]	2.000	39.000	.184
Sleep Deprivation	Pillai's trace	.168	3.939[a]	2.000	39.000	.028
	Wilks' lambda	.832	3.939[a]	2.000	39.000	.028
	Hotelling's trace	.202	3.939[a]	2.000	39.000	.028
	Roy's largest root	.202	3.939[a]	2.000	39.000	.028

Multivariate Tests

Sleep Dep 1=yes 0=no		Partial Eta Squared	Noncent. Parameter	Observed Power[b]
Control	Pillai's trace	.083	3.534	.348
	Wilks' lambda	.083	3.534	.348
	Hotelling's trace	.083	3.534	.348
	Roy's largest root	.083	3.534	.348
Sleep Deprivation	Pillai's trace	.168	7.877	.674
	Wilks' lambda	.168	7.877	.674
	Hotelling's trace	.168	7.877	.674
	Roy's largest root	.168	7.877	.674

Each F tests the multivariate simple effects of Time within each level combination of the other effects shown. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Exact statistic

b. Computed using alpha = .05

5. Sleep Dep 1=yes 0=no * Time

Estimates

Measure: MEASURE_1

Sleep Dep 1=yes 0=no	Time	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Control	1	.500	.159	.178	.822
	2	.500	.219	.057	.943
	3	.250	.177	-.109	.609
Sleep Deprivation	1	.182	.152	-.125	.489
	2	.455	.209	.032	.877
	3	.545	.169	.203	.887

Pairwise Comparisons

Measure: MEASURE_1

Time	(I) Sleep Dep 1=yes 0=no	(J) Sleep Dep 1=yes 0=no	Mean Difference (I-J)	Std. Error	Sig.[a]
1	Control	Sleep Deprivation	.318	.220	.156
	Sleep Deprivation	Control	-.318	.220	.156
2	Control	Sleep Deprivation	.045	.303	.881
	Sleep Deprivation	Control	-.045	.303	.881
3	Control	Sleep Deprivation	-.295	.245	.235
	Sleep Deprivation	Control	.295	.245	.235

Pairwise Comparisons

Measure: MEASURE_1

Time	(I) Sleep Dep 1=yes 0=no	(J) Sleep Dep 1=yes 0=no	95% Confidence Interval for Difference[a]	
			Lower Bound	Upper Bound
1	Control	Sleep Deprivation	-.126	.763
	Sleep Deprivation	Control	-.763	.126
2	Control	Sleep Deprivation	-.567	.658
	Sleep Deprivation	Control	-.658	.567
3	Control	Sleep Deprivation	-.791	.200
	Sleep Deprivation	Control	-.200	.791

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

Univariate Tests

Measure: MEASURE_1

Time		Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
1	Contrast	1.061	1	1.061	2.093	.156	.050
	Error	20.273	40	.507			
2	Contrast	.022	1	.022	.023	.881	.001
	Error	38.455	40	.961			
3	Contrast	.915	1	.915	1.451	.235	.035
	Error	25.205	40	.630			

Univariate Tests

Measure: MEASURE_1

Time		Noncent. Parameter	Observed Power[a]
1	Contrast	2.093	.292
	Error		
2	Contrast	.023	.052
	Error		
3	Contrast	1.451	.217
	Error		

Each F tests the simple effects of Sleep Dep 1=yes 0=no within each level combination of the other effects shown. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Computed using alpha = .05